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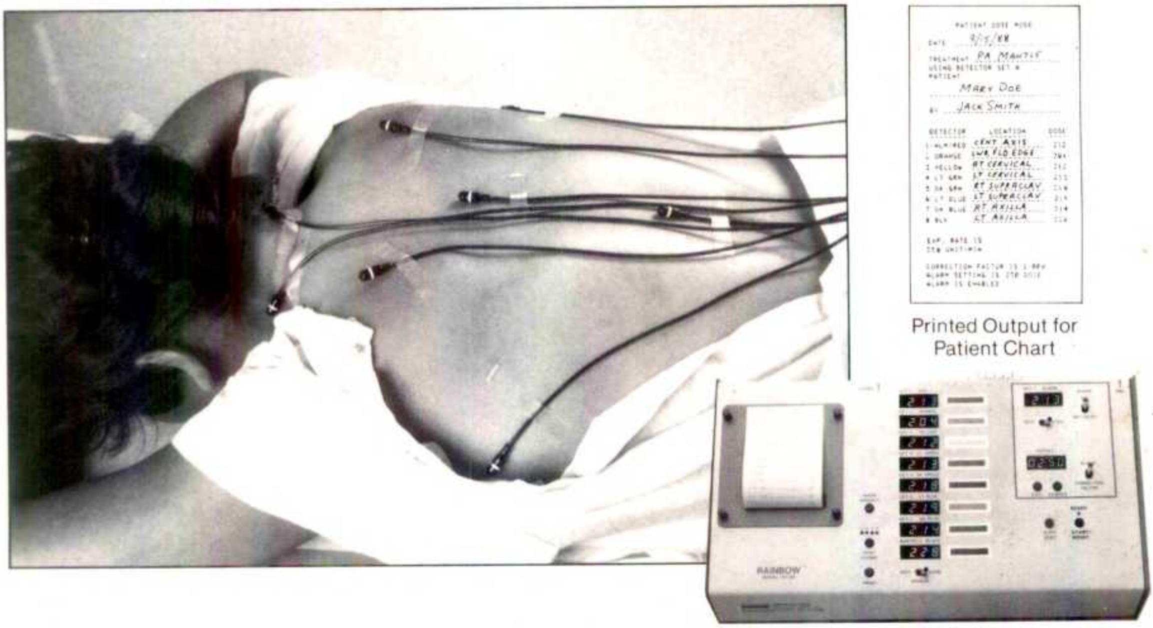

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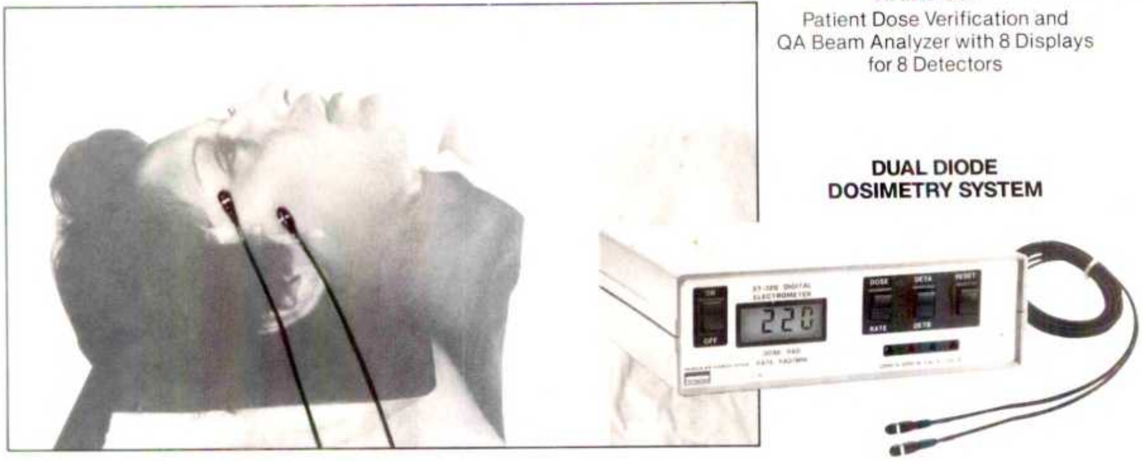

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VOL 63 NO 748 APRIL 1990

The British Journal of Radiology

Contents

Review

Page

Past and revised risk estimates for cancer induced by irradiation and their influence on dose limits 235
R. B. Richardson

Papers

Ultrasound evaluation of ectopic pregnancy including correlation with human chorionic gonadotrophin levels 246
S. E. Chambers, B. B. Muir and N. G. Haddad

The role of the STIR sequence in magnetic resonance imaging examination of bone tumours 251
R. Golfieri, H. Baddeley, J. S. Pringle and R. Souhami

The computed tomographic appearances and clinical significance of intussusception in adults with malignant neoplasms 257
J. G. Lorigan and R. A. DuBrow

Does scrotal ultrasound reduce the need for orchidectomy in the clinically malignant testis? 263
S. J. Milner and S. C. P. Blease

The range of bone density in normal British women 266
M. L. Hall, J. Heavens, I. D. Cullum and P. J. Ell

Clinical study of relative biological effectiveness for cervical carcinoma treated by ^{252}Cf neutrons and assessed by histological tumour eradication 270
Y. Maruyama, J. M. Feola, J. Wierzbicki, J. R. van Nagell, D. Powell and J. Yoneda

The effect of secondary electron spread on the penumbra in high energy photon beam therapy 278
M. J. Day, G. D. Lambert and S. M. Locks

Response of murine small intestine to combined treatment with fostriecin and X rays 286
K. R. Rao and H. Fritz-Niggli

The use of small fraction numbers in high dose-rate gynaecological afterloading: some radiobiological considerations 290
R. G. Dale

Technical notes

Peripheral doses of two linear accelerators employing universal wedges 295
B. J. McParland

Neutron and gamma ray measurements carried out around a Varian Clinac 2500 linear accelerator 298
W. A. Beckham

Case reports

Mammographic depiction of Poland's syndrome 302
R. A. Cooper and M. S. Johnson

Spontaneous disappearance of tuberculous psoas abscess calcification 303
S. C. Whitaker, B. J. Preston and H. McKim-Thomas

Osteosarcoma: an unusual metastasis 304
M. J. Charig, S. J. Golding and D. R. M. Lindsell

Pneumonia, diagnosed on the abdominal radiograph, as a cause for acute abdomen in children 306
P. A. S. Spencer

Congenital indifference to pain mistaken for non-accidental injury 308
J. A. Spencer and D. K. Grieve

Case of the month

A diaphragmatic nick 311
M. J. Broderick and A. M. Whyte

Short Communication

Medicolegal aspects of medical radiation exposure 313
W. M. Ross

Correspondence

Final Report of the BIR fractionation study 315
G. H. Fletcher
Authors' reply 315
G. Wiernik, C. J. Alcock, J. F. Fowler, J. L. Haybittle, J. W. Hopewell and M. Rezvani
Sedation for CT examinations in children 316
B. J. Cremin
The influence of tube type and operator experience on performance of small bowel enema 316
C. Bartram
Alterations in body and skin temperatures caused by MRI 317
J. A. Dennis and R. D. Saunders
Authors' reply 317
F. G. Shellock, D. J. Schaefer and J. V. Crues

Proceedings

Proceedings of the British Journal of Radiology

Imaging in abdominal sepsis, 19 October 1989 318
Vascular effects in tumour therapy, 10 November 1989 319

Book reviews

Craniospinal magnetic resonance imaging. *S. J. Pomeranz* 324
Bone mineral measurements by photon absorptiometry: methodological problems. *J. Dequeker, P. Geusens and H. W. Wahner* (Eds) 324

BIR Bulletin *facing page* 324

Featured in the next issue

Thyroid imaging using positron emission tomography — a comparison with ultrasound imaging and conventional scintigraphy in thyrotoxicosis
M. A. Flower, A. T. Irvine, R. J. Ott, F. Kabir, V. R. McCready, C. L. Harmer, H. L. Harmer, H. L. Sharma and A. G. Smith

The ultrasound cystodynamogram — a new radiological technique
A. E. Boothroyd, P. J. Dixon, T. J. Christmas, C. R. Chapple and D. Rickards

Oropharynx carcinoma: irradiation alone *versus* induction chemotherapy plus irradiation — 5 year results
G. Calais, A. Reynaud-Bougnoux, G. Garand, P. Beutter and O. Le Floch

Silicone implant to prevent visceral damage during adjuvant radiotherapy for retroperitoneal sarcoma
A. B. S. Ball, A. Cassoni, R. M. Watkins and J. Meirion Thomas

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ISSN 0007 1285

VOL 63 NO 749 MAY 1990

The British Journal of Radiology

Contents

Papers

Page

Thyroid imaging using positron emission tomography—a comparison with ultrasound imaging and conventional scintigraphy in thyrotoxicosis 325
M. A. Flower, A. T. Irvine, R. J. Ott, F. Kabir, V. R. McCready, C. L. Harmer, H. L. Sharma and A. G. Smith

The ultrasound cystodynamogram—a new radiological technique 331
A. E. Boothroyd, P. J. Dixon, T. J. Christmas, C. R. Chapple and D. Rickards

Congenital biliary dilatation: a spectrum of disease detailed by ultrasound 333
W. Young, C. Blane, S. J. White and T. Z. Polley

The role of dacryocystography in the management of patients with epiphora 337
J. Nixon, I. W. J. Birchall and J. Virjee

Oropharynx carcinoma: irradiation alone *versus* induction chemotherapy plus irradiation—5 year results 340
G. Calais, A. Reynaud-Bougnoux, G. Garand, P. Beutter and O. Le Floch

Silicone implant to prevent visceral damage during adjuvant radiotherapy for retroperitoneal sarcoma 346
A. B. S. Ball, A. Cassoni, R. M. Watkins and J. Meirion Thomas

The effect of Captopril on benign and malignant reactions in irradiated rat skin 349
W. F. Ward, A. Molteni, C. Ts'ao and J. M. Hinz

Technical note

The variation of wedge factors with field size on a linear accelerator 355
S. J. Thomas

Case reports

Calcification of the large bowel in schistosomiasis demonstrated by computed tomography 357
M. Al-Hindawi, G. H. Whitehouse, A. G. Al-Ansari, H. Kamel and C. R. Soni

Malignant struma ovarii: presentation and management 360
M. E. A. O'Connell, C. Fisher and C. L. Harmer

Tuberculosis of the patella 363
P. Shah and R. Ramakantan

Raynaud's disease in childhood with radiological features 364
T. Shono, K. Okadome, G. Naritomi and S. Suita

Case of the month

A Chinese puzzle 367
J. W. Williams and M. C. Collins

Correspondence

Can ultrasound replace the intravenous urogram? 369
J. A. Spencer, D. R. M. Lindsell and I. Mastorakou

Proceedings

Proceedings of The British Institute of Radiology

What shall we do about osteoporosis? 22 November 1989 370
Radiation protection: sense or nonsense? 13 December 1989 373

Proceedings of the British Medical Ultrasound Society
21st Annual Meeting, 5–7 December 1989 377

Book reviews

Radiation therapy of head and neck cancer. *G. E. Laramore* (Ed.) 408
Multimodal treatment of ovarian cancer, EORTC Vol. 20. *P. F. Conte, N. Ragni, R. Rosso and J. B. Vermorken* (Eds) 408
Pediatric Radiation Oncology. *E. C. Halperin, L. E. Kun, L. S. Constine and N. J. Tarbell* 408
A primer on theory and operation of linear accelerators in radiation therapy. *C. J. Karzmark and R. J. Morton* 408
Determination of dose equivalents from external radiation sources, Part 2. ICRU Report 43 409
Tissue substitutes in radiation dosimetry and measurements. ICRU Report 44 409
Hospital radiopharmacy principles and practice. IPSM Report No. 56. *M. Frier, J. G. Hardy, S. R. Hesselwood and R. Lawrence* 409
Diagnostic ultrasound. Principles, instruments and exercises, 3rd edn. *F. W. Kremkau* 410

BIR Bulletin *facing page* 410

Featured in the next issue

Recent advances and future projections in clinical radionuclide imaging (Review article)
A. M. Peters

Ultrafast magnetic resonance scanning of the liver with echo-planar imaging
M. K. Stehling, R. M. Charnley, A. M. Blamire, R. J. Ordidge, R. Coxon, P. Gibbs, J. D. Hardcastle and P. Mansfield

Further studies on selective radioprotection by organic zinc salts and synergism of aspartate with WR 2721
G. L. Floersheim and A. Bieri

A comparison of two methods of *in vivo* dosimetry for a high energy neutron beam
S. W. Blake, D. E. Bonnett and J. Finch

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ISSN 0007 1285

VOL 63 NO 751 JULY 1990

The British Journal of Radiology

Contents

Review

Page

Urinary tract infection in paediatrics: the role of diagnostic imaging 507
I. Gordon

Papers

Imaging for cochlear implants 512
P. D. Phelps, J. A. D. Annis and P. J. Robinson

Initial experience with percutaneous transluminal angioplasty in the management of Takayasu's arteritis 517
S. Sharma, M. Rajani, U. Kaul, K. Talwar, V. Dev and S. Shrivastava

Evaluation of response to chemotherapy of human cystic echinococcosis 523
T. Todorov, K. Vutova, G. Mechkov, D. Petkov, G. Nedelkov and Z. Tonchev

Bacterial contamination of contrast media stored after opening 532
D. Lisle, J. F. Ratcliffe, J. Faoagali and S. Cherian

Assessment of a single lumbar spine radiograph in low back pain 535
S. Padley, F. Gleeson, R. Chisholm and J. Baldwin

Skeletal abnormalities in Refsum's disease (heredopathia atactica polyneuritiformis) 537
G. R. Plant, D. M. Hansell, F. B. Gibberd and M. C. Sidey

The effect of ultrasound on the cytoxicity of adriamycin 542
P. Loverock, G. ter Har, M. G. Ormerod and P. R. Imrie

Comparison of 5-Fluorouracil pharmacokinetics following intraperitoneal and intravenous administration using *in vivo* ^{19}F magnetic resonance spectroscopy 547
J. Glaholm, D. Collins, B. Al-Jehazi, J. C. Sharp, J. Adach, A. Hind, V. R. McCready, H. White and M. O. Leach

Smoking and mucosal reactions to radiotherapy 554
T. Rugg, M. I. Saunders and S. Dische

Glutathione and crysteine levels in human tumour biopsies 557
M. Guichard, F. Lespinasse, R. Estelin, A. Gerbaulet, C. Haie, E. Lartigau, E. P. Malaise, C. Micheau, M. Prade, J. M. Richard and P. Weeger

Technical notes

Cylindrical forms of isodoses in gynecological afterloading therapy: an atlas using the Buchler afterloading machine 562
M. Busch II and E. Dühmke

Quality assurance of viewing boxes: proposal for establishing minimum requirements and results from a Spanish quality control programme 564
E. Guibelalde, E. Vañó and A. L. Llorca

Case reports

Intracardiac extension of Wilms' tumour: demonstration by magnetic resonance 568
J. M. Gibson, M. A. Hall-Craggs, C. Dicks-Mireaux and J. P. Finn

Difficulties in the diagnosis of metastatic testicular teratoma 569
R. Huddart, N. R. Moore, M. V. Williams and A. K. Dixon

Cytomegalovirus infection masquerading as colonic neoplasia 573
H. G. Lewis-Jones, R. G. Ward and C. Garvey

Pathological fracture of the femoral shaft in a case of Servelle–Martorell syndrome (phleboeclatic osteohypoplastic angiodysplasia with associated anterio-venous malformation) 574
W. W. Gibbon and J. Pooley

Epidural abscess of the cervical spine: case report and literature review 576
J. W. Williams and T. Powell

Primary osteosarcoma of the uterus 578
M. G. Caputo, K. L. Reuter and F. Reale

Case of the month

Just another case of varicose veins? 581
R. C. Travis, D. M. Rowan and J. Miller

Correspondence

Dysphagia after fast neutron therapy to head and neck 583
W. Duncan and A. J. Munro

Intraluminal irradiation in oesophageal tumours using the high-dose-rate Microselectron 583
J. H. Hay and A. D. Flores

Quality assurance of ultrasound test objects 584
P. D. Brannigan and T. K. Bell

Proceedings of the British Institute of Radiology 585
Radiobiology proffered papers, 23 February 1990

Book reviews

Introduction to neuroimaging. *W. M. Orrison* 589
Mammography. Exercises in radiological diagnosis *P. Haehnel and C. Kleitz* 589
Bone and joint imaging. *D. Resnick* 589
Panoramic radiology, 2nd edn. *O. E. Langland, R. P. Langlais, W. D. McDavid and A. M. DelBalso (Eds)* 589
Small bowel radiology. Introduction and atlas. *G. Antes and F. Eggemann* 589
X-ray differential diagnosis in small bowel disease: a practical approach. *J. L. Sellink* 590
Diagnosis and therapy of fetal anomalies. Clinics in diagnostic ultrasound. *J. C. Hobbins and B. R. Benacerraf (Eds)* 590

BIR Bulletin *facing page* 590

Featured in the next issue

Quantitative microfocal radiography of children with renal osteodystrophy; comparison with laboratory and histological findings
J. C. Buckland-Wright, M. W. Spring, R. H. K. Mak, C. Turner, J. Compston, S. Vedi, G. B. Haycock and C. Chantler

Magnetic resonance of diseased skeletal muscle: combined T_1 measurement and chemical shift imaging
A. E. Lamminen, J. I. Tanttu, R. E. Sepponen, I. J. I. Suramo and H. Pihko

An investigation into the performance of an automated quality assurance and dosimetry system in diagnostic radiology
C.-L. Chapple, K. Faulkner and R. M. Harrison

Transforming growth factor beta: a promoter of late connective tissue injury following radiotherapy
P. A. Canney and S. Dean

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The British Journal of Radiology

Review article

Past and revised risk estimates for cancer induced by irradiation and their influence on dose limits

By R. B. Richardson, BSc, MSc

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(Received June 1989 and in revised form October 1989)

The present is a time of great change in the assessment of radiation risk and its influence on dose limits. The main sources of risk estimates arise from irradiation for medical reasons and from the use of atomic weapons. The effects of radiation on humans and animals are reviewed by such august bodies as the International Commission on Radiological Protection (ICRP), the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and the Biological Effects of Ionizing Radiation (BEIR) Committee in the USA. Over the years they have developed many of the concepts that give structure to the science of limiting radiation-induced cancers and other harmful effects. These concepts are mentioned here for completeness and because they also provide relative stability in a time of change.

Central in its importance on radiation risk estimates is the analysis of excess cancer risks of the Japanese bomb survivors which was based on a dosimetry system (T65DR) devised in 1965. Reassessment commenced in the early 1970s, with a new dosimetry system employed in the extended study of the Nagasaki and Hiroshima populations in 1985. The considerable debate that the new "DS86" dosimetry of the Japanese Life Span Study has caused reminds us again of the key position of this Japanese population in influencing radiation risk estimates and protection regulations.

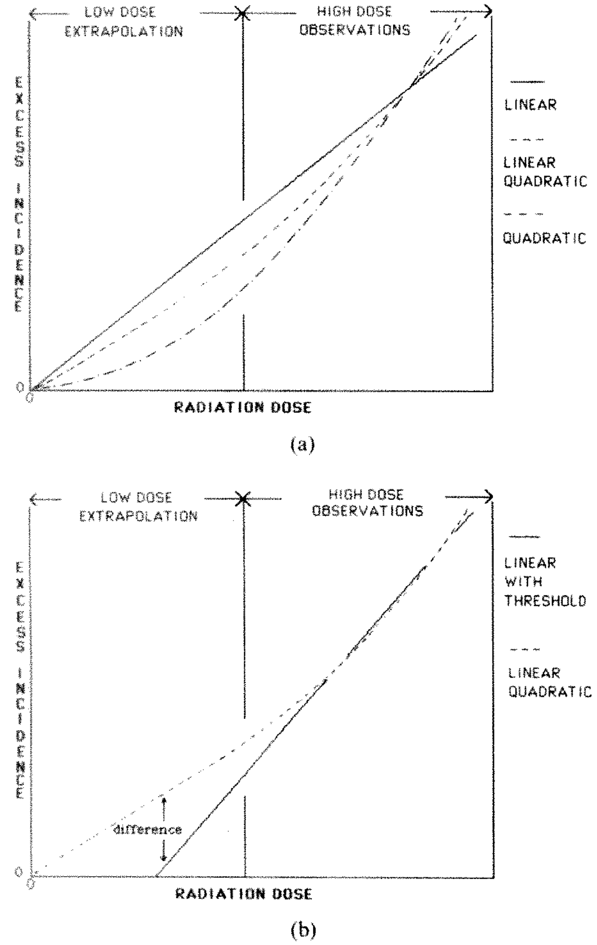
Historical studies and concepts

Five years after his discovery of radioactivity, Becquerel in 1901 found that a glass-tube of 200 mg of radium, carried in his vest pocket, caused a red and blistered skin. This was an observation of a "somatic effect" of radiation, which is expressed in the exposed individual; others discovered later include skin tumours and other cancers among the early radiologists (Medical Research Council, 1956; Smith & Doll, 1981). Besides somatic radiation effects, such as certain cancers and developmental abnormalities, there are hereditary effects, which are expressed in the descendants of the exposed person.

In 1977 the ICRP in its Publication 26 gave, for radiation protection purposes, a risk coefficient for radiation-induced total fatal cancers, excluding hereditary effects, of about 1.25×10^{-2} Sv^{-1} (1.25 in 100 people per unit of effective dose equivalent) for the general population. The risk of fatal leukaemia was estimated at 0.2×10^{-2} Sv^{-1} based on a ratio of about one leukaemia relative to five cases of non-leukaemia cancers. The risk estimates are for low dose, low dose-rate exposure for the population in general, and give no indication of the differences in sensitivity to radiation owing to age and sex. Most radiation risk data are derived from high dose exposures, and have been extrapolated to low doses for radiation protection purposes. Risk estimates given in ICRP 26 (1977) assume a linear dose response with no threshold and with some risk of cancer and hereditary defects no matter how small the dose. The linear model was adopted, because it was the most cautious, in preference to linear-quadratic or quadratic relationships, which are other possibilities predicted by theoretical modelling of cancer induction (Fig. 1).

Cancer risk is given per unit dose equivalent (sievert) where a "quality factor" has been used to take account of the varying biological effectiveness of different radiations. The quality factors (Q) given by ICRP 26 (1977) are 1 for beta and gamma rays, 2.3 and 10 for slow and fast neutrons, and 20 for alpha-particles; currently the Qs for neutrons are under review. Risk estimates are given per sievert (Sv) where dose equivalent = absorbed dose (Gy) × Q.

The risk of excess fatal cancers per Sv varies for different organs and tissues of the body. ICRP 26 (1977) gave risk weighting factors which allow for the contribution made by each organ to the total risk when the whole body is irradiated. Table I gives the average values to a mixed population of all ages and both sexes. The radiation risks and weighting factors for particular



(a)

(b)

Figure 1. (a) Dose-response curves for three models, showing high dose risk observations extrapolated to give the excess incidence expected for low dose exposures. (b) Hypothetical comparison of the linear-quadratic model without threshold and the linear model with threshold. Comparative agreement is shown at high doses. The difference in the predicted excess incidence for low doses is shown.

Table I. Organ weighting factors and the risk of cancer induction

Tissue or organ	Risk of cancer induction (10^{-2} Sv^{-1})		Weighting factors (fatal cancers and hereditary effects)
	Incidence	Fatality	
Red bone marrow (leukaemia)	0.21	0.20	0.12
Breast	0.40	0.25	0.15
Lung	0.21	0.20	0.12
Thyroid	1.05	0.05	0.03
Bone surfaces	0.06	0.05	0.03
Skin	1.01	0.01	0
Remainder	0.65	0.50	0.30
Total	3.6	1.25	0.75
Gonads (hereditary effects first two generations)		0.40	0.25
Whole body total		1.65	1.00

Weighting factors and fatal risk are from ICRP 26 (1977) and incidence from ICRP 45 (1985) with no attempt made to revise these figures in accordance with the new DS86 dosimetry.

groups, such as for females, males, the fetus, children and elderly people, will differ significantly from ICRP risk estimates and weighting factors chosen for radiation protection purposes (Beninson & Sowby, 1985).

The weighting factors are useful for estimating the effects of partial or non-uniform whole-body irradiation. The same risk of cancers and hereditary defects resulting from irradiation of the lung alone, for example, can be compared with an equivalent irradiation of the whole body. The equivalent whole body irradiation, in units of effective dose equivalent (Sv), is derived as the product of the dose equivalent (Sv) to the lung and the appropriate weighting factor, in this case 0.12. Thus a unit dose of whole-body irradiation would give the same overall risk as a dose eight times (1/0.12) greater to the lungs alone. This means that the implied dose limits to individual organs and tissues can be higher than the 50 mSv UK legal annual dose limit for whole-body irradiation, subject to the dose equivalent limit for individual organs and tissues of 500 mSv (employees aged 18 years or over, Ionizing Radiations Regulations, 1985).

Studies investigating the induction by radiation of hereditary disease in humans have failed to show statistically significant increases in hereditary defects. Risk data have been inferred from animal studies, mainly from the doubling dose for genetic disease obtained from experiments on mice (UNSCEAR, 1977; BEIR III, 1980). The average risks, to a specified population, of serious hereditary defects in the first two generations has been estimated by ICRP 26 (1977) as 0.4×10^{-2} Sv^{-1}; and 0.8×10^{-2} Sv^{-1} for all future generations. The UNSCEAR (1986) report reviewed the data on hereditary effects of radiation and reduced these estimates by 35% because of the reduced risk of Down's syndrome; however, no estimates were given for multifactorial diseases such as ankylosing spondylitis and schizophrenia. The UK's National Radiological Protection Board (NRPB) continues to adopt 0.8×10^{-2} Sv^{-1} for all generations, which is now quoted in preference to the risk to the first two generations.

The risk factors for cancer incidence are, of course higher than for cancer deaths, as some radiation-induced cancers have a low mortality. As indicated in Table I, thyroid cancer mortality is about 5–10%, breast cancer mortality about 40–50%, while mortality from lung cancer is almost 100%. The total incidence of cancer after exposure of the general population comes to about three times the risk of inducing a fatal cancer (ICRP 26, 1977 data). The risks for both cancer incidence and mortality are higher in women than in men. Breast cancer is virtually confined to women and thyroid cancer is two to three times more common in women than in men.

Cancers and hereditary defects were identified in ICRP 26 (1977) as being stochastic (random) effects of radiation, that is having no threshold in dose and no change in severity with dose (only the incidence is a function of dose). On the other hand, cataracts and impaired fertility are examples of non-stochastic (non-random) effects, namely having a threshold and changing in severity with dose. The certainty that radiation effects can be rigidly categorized into one or other group is falling into disfavour (Mays, 1988). Skin cancer is a malignancy that has been shown to have threshold characteristics in mice (Fry et al, 1986). In an area of considerable debate, concerning the risk of mental retardation from radiation exposure of the fetus, the cautious position is to accept that the risk is a linear function, but without the expected "non-stochastic" threshold (Stather et al, 1988).

The influence of acceptability and cost on dose limits

Aspects of the acceptability of radiation risk were considered by ICRP 26 (1977) and later by The Royal Society (1983). The Royal Society concluded that the maximum acceptable annual risk of excess fatality of an individual worker was 10^{-3} whilst that for a member of the public was around 10^{-5}. A later report by the UK's Health and Safety Executive (1988) considered that the limit of tolerable risk to the public was 10^{-4}, a factor of 10 larger than the Royal Society's estimate.

The economic cost of radiation protection measures (Fleischmann & Webb, 1986; Russell, 1986; NRPB, 1986) influences radiation regulations. The requirement that all doses should be "as low as reasonably achievable" (ALARA) is a balance between economic resources and social expectations. The current NRPB advice, based on its own interim cost–benefit analysis, is that the baseline cost of radiation protection measures are £10 000 and £30 000 Sv^{-1} for the general public and for workers respectively.

Dose limits take into account estimates of radiation risk per sievert and levels of acceptability. The current dose limits for both those occupationally exposed to ionizing radiation and for the general public are specified in the UK by the Ionizing Radiation Regulations (1985). These regulations are based on the recommendations of ICRP 26 (1977). The current *legal* annual dose limits are 50 mSv for workers and 5 mSv for individual members of the public, although the ICRP statement from the 1985 Paris meeting recommended that the average annual effective dose equivalent over a lifetime should not exceed 1 mSv in a year. This results in risks, on the basis of the 1965 Japanese dosimetry (T65DR), being within acceptable limits as defined by the Health and Safety Executive.

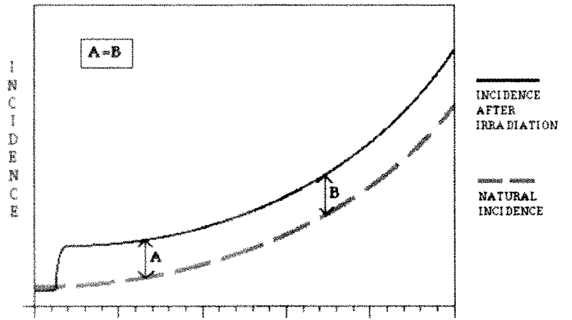
The new Japanese bombing dosimetry (DS86) and its influence

Radiation risk estimates have been derived from many studies, including patients treated for anklylosing spondylitis (Darby et al, 1987), cervical cancer (Boice et al, 1985) and tinea capitus (Ron et al, 1988), medical use of Thorotrast (BEIR III, 1980), workers in the radium luminizing industry and American radiologists (BEIR III, 1980), among others. A very influential study is that concerning the 90 000 survivors of the Japanese bombings.

In the late 1970s it was suggested that there were serious inadequacies in the T65DR dosimetry system for the Hiroshima and Nagasaki bombings. The new DS86 dosimetry takes into account changes to the gamma ray and neutron kerma. In addition there has been further follow-up from 1975 to 1985. A report by Preston and Pierce (1987) reassessed the effect of the atomic bomb radiation dosimetry and estimated that the risk estimates, using D586 dosimetry, increased follow-up and the relative risk model, for leukaemia and non-leukaemia cancer mortality are 75–85% higher (with allowance made for possible non-linearity at the higher doses) than by the T65DR dosimetry and absolute risk model. The ICRP Como Statement (1987) indicated that a preliminary reassessment of the Hiroshima and Nagasaki survivors had raised the fatal cancer risk estimate by a total factor of the order of 2. This change is for a population of all ages whereas, for a worker population of ages 18–65 years, the ICRP stated the change will be smaller. The ICRP did not consider this sufficient at that stage to warrant a change in dose limits for occupational exposure. The ICRP also noted that two further factors, the precise form of the dependence of excess risk with time after exposure and the shape of the dose–response curve, could, if established, result in larger changes being adopted later.

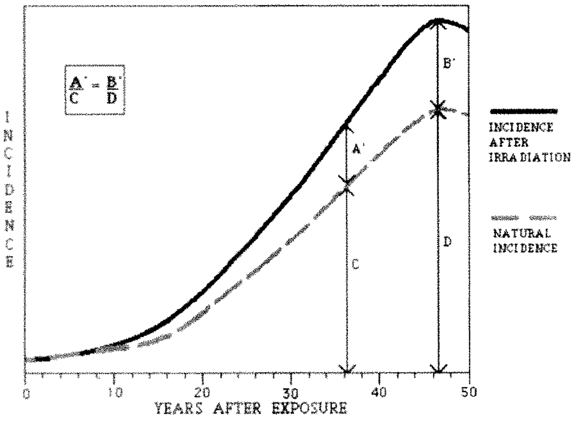
The NRPB (1987) considered the ICRP Como Statement and soon after issued guidance on the implications of changes in risk estimates. In their view, the DS86 dosimetry and longer follow-up increased the risk of inducing a fatal cancer, as given by ICRP 26 (1977), by a factor of 2–3. The acceptance of the higher risk estimates, at the 1985 dose limits, predicted annual fatalities to the UK public and workers that verged on the unacceptable as judged by criteria of The Royal Society Study Group (1983). As a result, the NRPB *recommended,* as interim guidance on dose limits before any legal changes based on future ICRP recommendations, that the total dose to individual members of the public should not exceed an average annual effective dose equivalent of 1 mSv. The contribution from current discharges from a single site, such as a nuclear power station, should not exceed 0.5 mSv $year^{-1}$. The NRPB also recommended that exposure to occupational workers be controlled so as not to exceed a time-averaged dose equivalent of 15 mSv $year^{-1}$.

The 1986 dosimetry differs from that of 1965 in that the neutron component is reduced because of allowances for humidity over Hiroshima and Nagasaki, ABSOLUTE/ADDITIVE MODEL (LEUKAEMIA)



(a)

RELATIVE/MULTIPLICATIVE MODEL (SOLID CANCERS)



(b)

Figure 2. Schematic representations showing the simplified variation of excess incidence for a population aged 30–39 years at the time of exposure by (a) a constant absolute (additive) risk model applied to leukaemia and (b) a consultant relative (multiplicative) risk model as applied to solid cancers.

changes in shielding factors for buildings and organ transmission factors. These modifications have resulted in minor changes to risk estimates. It has been the extension of the follow-up period and the different form of extrapolating from a 40 year study to the survivors' entire lifetimes that have caused major changes in risk estimation (Shimizu et al, 1987).

As two-thirds of the Japanese survivors are still alive, it is necessary to extrapolate the excess cancers that have been observed to a lifetime's experience. Previously, the Japanese bombing risk estimates employed an absolute (additive) risk model for all cancers, where the annual excess risk due to irradiation remained constant with time (Fig. 2a). UNSCEAR (1988) suggests, stating reservations, that a relative (multiplicative) model is more likely for most solid cancers. The multiplicative model in its simplest form determines the excess cancers by applying a constant multiplying factor to the age-dependent incidence of natural cancers in the population (Fig. 2b). The natural cancer rates of a control unexposed population increase rapidly with age; therefore the relative risk model predicts a higher number of excess cancers, and therefore a higher risk, than the absolute model. For the general Japanese population, the 1988 UNSCEAR report derives fatal cancer risks, based on the relative risk model, for high dose and high-dose rate X-ray and gamma-ray exposures. The risk was calculated as 11×10^{-2} Gy^{-1} using age-specific risk coefficients, which is about twice that of the absolute model.

Table II. Estimated excess incidence and fatal cancer risks in a UK population (all ages, both sexes) associated with exposure to low dose, low dose-rate whole-body irradiation, taking into account the DS86 dosimetry (Stather et al, 1988). (The percentage fatalities are from ICRP (1985) and OPCS (1981))

Cancer	Percentage fatality	Cancer risk (10^{-2} Sv^{-1})		Fraction of total risk
		Incidence	Fatality	
Leukaemia	90	0.31	0.28	0.05
Breast	50	1.1	0.55	0.10
Lung	95	1.3	1.2	0.23
Thyroid	10	0.25	0.025	0.005
Bone	80	0.065	0.05	0.009
Liver	95	0.16	0.15	0.03
Colon	75	0.49	0.37	0.07
Stomach	95	0.25	0.24	0.05
Skin	1	1.00	0.01	0.002
Remainder	75	2.17	1.63	0.31
Total		7.1	4.5	0.85
Hereditary effects (all future generations)			0.8	0.15
Whole body total			5.3	1.00

It is more relevant to workers and the public to know of the low dose, low dose-rate radiation risks that they more probably face. The incidence of human cancers of the thyroid, breast and leukaemia appear to increase linearly with dose, without threshold. However, comparable X-ray and gamma-ray exposures of animals have shown a dose-rate dependency for cancer induction. A dose-rate effectiveness factor (DREF) of 2 was used by the ICRP in 1977 to reduce high dose, high dose-rate risk estimates to those more appropriate for radiological protection purposes. A DREF of 3 has been adopted by the NRPB for all cancers (except a DREF of 2 for breast cancer) to reduce high dose, high dose-rate risk estimates to those appropriate for low dose (< 10 mGy), low dose-rate (< 100 mGy d^{-1}) conditions (Stather et al, 1988).

To compute risk coefficients for radiation-induced fatal cancer in the UK population, Stather et al (1988) employed an absolute risk model for leukaemia, thyroid, bone and liver cancer, and an age-specific relative risk model for other cancers (Table II). The incidences of induced leukaemia and the majority of other cancers were estimated from Japanese A-bomb survivors (Shimizu et al, 1987, 1988). The total lifetime fatal cancer risk following uniform whole-body irradiation of the UK public at low doses and low dose rates is given as 4.5×10^{-2} Sv^{-1}, which is $3\frac{1}{2}$ times the ICRP 26 (1977) estimates. The fatal cancer risk estimate for a UK working population (ages 20–64 years, both sexes) is 3.4×10^{-2} Sv^{-1}. These risk estimates at the NRPB interim dose limits of 1.0 mSv and 15 mSv, to the public and to workers respectively, give rise to annual risks which fall within the Health and Safety Executive's criteria of tolerable risk. The estimated total incidence of radiation-induced cancer is about $1\frac{1}{2}$ times the fatal cancer risk. Added to these risks is the 0.8×10^{-2} for serious hereditary defects for all future generations.

Taking account of the DS86 dosimetry, this model for the UK general population predicts that the ratio of fatal solid cancers to leukaemias is about 15:1, compared with 5:1 by ICRP 26 (1977) (Table I). Greater risks for lung and breast are also predicted. Lung cancer is 0.23 as a fraction of the total radiation cancers and hereditary defects, compared with the ICRP 26 (1977) lung weighting factor of 0.12.

Radiation risk and age at exposure

Age is the critical factor in determining radiation risk. Proliferating cells are more susceptible to the induction of cancer, and it is during fetal development and childhood that intense tissue generation and differentiation takes place. For children and adults, whatever the age at exposure, the excess solid tumours commonly occur at ages comparable with those at which spontaneous tumours appear at the same site (UNSCEAR, 1988).

The rapid growth of the embryo and fetus could be expected to make them highly susceptible to radiation-induced cancer. Animal experiments have failed to find a particular sensitivity (UNSCEAR, 1986). However, association between pre-natal X rays and childhood cancer has been shown by the Oxford Survey of Childhood Cancer (Stewart & Kneale, 1970), the study of the Oxford Survey's dizygotic twins by Mole (1974) and by Monson and MacMahon (1984) in the USA. Children exposed *in utero* are subject to an estimated total incidence of excess cancers of 6×10^{-2} Sv^{-1} (BEIR III, 1980) of which nearly half this risk can be assumed to be for leukaemia. In recent years, the mortality of childhood cancers has been reduced to approximately 50% (OPCS, 1981).

Exposure *in utero* has been shown to be associated with severe mental retardation (Otake & Schull, 1984; Mole, 1987). The fetus is most sensitive to this effect during the period 8–15 weeks of gestation and the incidence is now assumed to be 45×10^{-2} Sv^{-1} (Stather et al, 1988) with some evidence for a threshold dose in the region 0.2–0.4 Gy (Otake et al, 1988). Serious mental retardation also results from exposure during weeks 16–25, but at about a quarter of the frequency, with a threshold of about 0.6 Gy (Otake et al, 1988).

Table III. Age variation of the risk of radiation-induced fatal leukaemia for the UK population

Age group	Fatal leukaemia risk factor (10^{-2} Sv^{-1})	Ratio of leukaemia risk for age group compared with adults
Adults	0.28	1.0
Children over 10 years	0.35	1.3
Children 0–10 years	0.5	1.8
Unborn child	1.25	4.5

The leukaemia risks and ratios were compiled for childhood exposure and childhood leukaemia estimated by Stather et al, 1986, and for adult exposure, by Stather et al, 1988. The DS86 dosimetry has been taken into account.

There is convincing evidence from the atomic bombings and radiotherapy patients that children under 10 years old are more susceptible than adults to induction of cancers (Darby, 1986). Children are particularly susceptible to tumours of the thyroid, bone, bone marrow and breast (UNSCEAR, 1988). Studies of children exposed to high radiation doses for treatment of primary cancers suggest a 15 or more relative risk of a second cancer of any site. The cumulative probability of cancer by age 25 years is 3–12% with about 68% of all second tumours found in the field of the original radiation. Second tumours are frequently associated with radiation in children known to be genetically susceptible to cancer.

For the atomic bomb data, the latent period for leukaemia is related to age at exposure. For children under 10 years old, the latency is brief, beginning 3–5 years after exposure and reaching a peak 7–8 years later (Ichimaru & Ishimaru, 1975). Stather et al (1986) estimated the upper limits for the induction of radiation-induced fatal leukaemia for different age groups (Table III). The fetus is up to 4.5 times at greater risk of induced fatal leukaemia than an adult. The excess of other malignancies is less certain, as the extended data from the Japanese bombings show that the exposure of the fetus induces cancers not only in children but in adults also (Yoshimoto et al, 1988). It is self-evident that the weighting factors for selected age groups (as yet not available) will differ from those of the general population given in Tables I and II. There are major difficulties concerning age-related risk assessment from uncontrolled radiation exposures, such as occurred after the Japanese bombings and the Chernobyl accident. Risk estimates in the case of paediatric radiography may perhaps be obtained by recording comprehensive details of exposure, to aid the dosimetric assessment in any later study of radiation risk.

Fatal malignancies and genetic risk from irradiation are dependent on the sex of the individual and age at exposure (ICRP 27, 1977). Based on the absolute risk model and the T65DR dosimetry, Fig. 3 shows this variation from 20 years of age upwards, as there were,

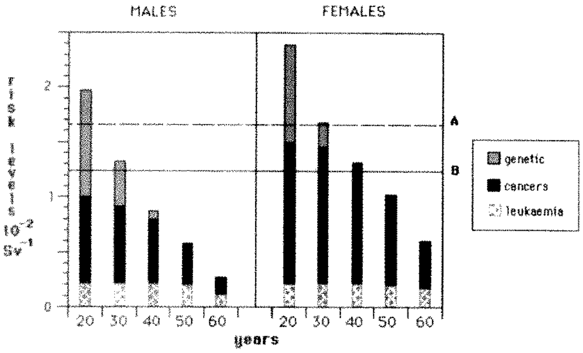


Figure 3. Age and sex dependence of fatal malignancy and genetic risks. B is the nominal total cancer risk and A is the total cancer plus genetic risk for the general population at 1.25 and 1.65×10^{-2} Sv^{-1} respectively adopted by ICRP 26 (1977) based on the old T65DR dosimetry, employing an absolute risk model (ICRP 27, 1977).

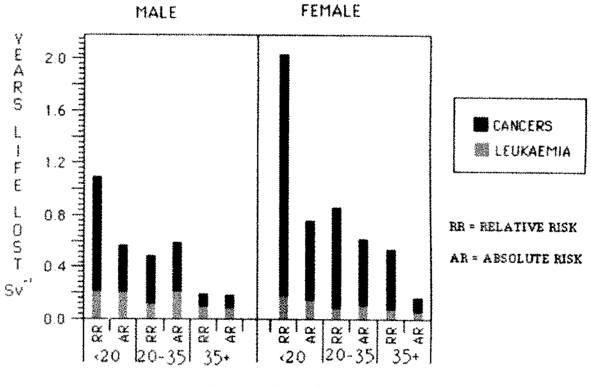


Figure 5. Age and sex dependence of years life lost based on relative risk (RR) and absolute risk (AR) models, for leukaemias and non-leukaemia cancers. Risk coefficients were derived from the DS86 bomb survivor data in the same manner as for Fig. 4 (Little & Charles, 1989).

and still are, limited data for the embryo, fetus and children. The trends shown still hold good. Genetic risk is greatest during the reproductive period of life of the young adult. There is a slight decrease in risk with age of exposure for leukaemia; this is marked for other cancers, owing to their long latent intervals in adults. The mean latency for radiation-induced leukaemia is in the region of 10–13 years, while that for most other cancers is at least twice as long.

On the basis of the increased sensitivity of the fetus and children, and of longer life expectancy, lower dose limits have been set for these groups than for adults. Trainees aged under 18 years have an annual dose limit of 3/10 of the 50 mSv whole body legal dose limit for employees aged 18 years or over (Ionizing Radiations Regulations, 1985). The dose limit for the abdomen of a woman of reproductive capacity who is at work is 13 mSv in any consecutive 3 month interval and, when pregnant, the dose limit is 10 mSv during the declared term of pregnancy.

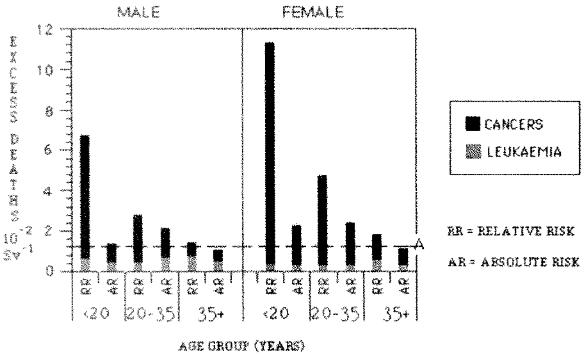


Figure 4. Age and sex dependence of fatal malignancies based on relative risk (RR) and absolute risk (AR) models, for leukaemias and non-leukaemia cancers. All risk coefficients for Figs 4 and 5 were derived from the DS86 bomb survivor data (Little & Charles, 1989) and radiation-induced excess cancer rates estimated using the 1986 England and Wales base cancer rates. A DREF of 3 was assumed to obtain the low dose, low dose-rate estimations shown. Figures 4 and 5 assume that leukaemias start 3 years after exposure and other cancers start 10 years after exposure. A is the nominal total cancer risk of 1.25×10^{-2} Sv^{-1} adopted by ICRP (1977), based on the old T65DR dosimetry.

Since the time when the data shown in Fig. 3 were collected, the changes in the DS86 dosimetry, the extended follow-up period and the use of the relative risk model have increased the risk estimates. Genetic risk, deduced from animal experiments, to two generations remains relatively unchanged. Little and Charles (1989) have estimated the cancer risks for three age groups of the UK population from the DS86 bomb survival data (Fig. 4). Besides giving the excess numbers of cancers as an index of harm, UNSCEAR (1988) also gave a second index, that of the loss of life expectancy. Using the relative risk model, Little and Charles (similar

Table IV. The average and the range of annual dose to the UK population from natural and artificial sources (Hughes et al, 1989)

Natural and artificial sources	Average (μSv)	Range (μSv)
Cosmic rays	250	200–300
Terrestrial gamma rays	350	100–1000
Internal irradiation	300	100–1000
Radon decay products	1200	300–100 000
Thoron decay products	100	50–500
Medical	300	
Fallout (bomb tests and Chernobyl)	10	
Occupational exposure	5	
Discharges	<1	
Miscellaneous (mostly air travel)	10	
Total	2500	

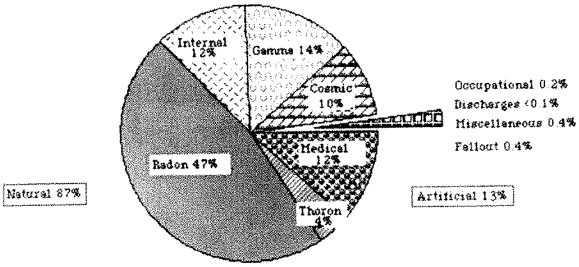


Figure 6. The average annual dose to the UK population, given as a percentage of the total exposure of 2.5 mSv (Hughes et al, 1989) (scaling is approximate).

to UNSCEAR, 1988) predict for both sexes and all ages, a total of two and half times more excess cancers than does the absolute model, whereas the ratio of years of lost life by the two models is about one and a half (Fig. 5). By the currently favoured relative risk model, the total excess cancer (including leukaemia) deaths and years of lost life for females is about one and a half times the risk for males.

Dose and risk estimates for natural and artificial radiation

The risk of radiation-induced cancers to a population is the sum of the risks from natural and artificial sources. The average annual dose to the UK population totals 2.5 mSv, with artificial sources comprising 13% of the total (Hughes et al, 1989; Clarke & Southwood, 1989) (Table IV, Fig. 6). It is important to estimate the risks of radiation exposure and place them in perspective with other hazards of everyday life (Pochin, 1980). Table V(a) gives the risk of death per year from common causes such as smoking and road accidents.

Table V. Average annual risk of death in the UK from (a) some common causes and (b) accidents in various industries and from cancers potentially induced among radiation workers

	Risk of death per year
(a) Common causes	
Smoking 10 cigarettes a day	1 in 200
Natural causes, 40 years old	1 in 700
Road accidents	1 in 10 000
Home accidents	1 in 10 000
Radiation exposure at a rate of 1 mSv per year	1 in 22 000
Accidents at work, all employment	1 in 50 000
(b) Industries	
Sea fishing	1 in 500
Coal mining	1 in 7000
Construction	1 in 10 000
Metal manufacture	1 in 17 000
Radiation workers (1.1 mSv year^{-1} average)	1 in 27 000
Textiles	1 in 28 000
Food, drink and tobacco	1 in 45 000
Timber, furniture, etc.	1 in 100 000
Clothing and footwear	1 in 300 000

Tables are modified and updated from NRPB's *Living with Radiation* (1989) (see Bibliography) with an average dose to radiation workers of 1.1 mSv year^{-1} (Hughes et al, 1989). A risk to the public of 4.5×10^{-2} year^{-1} was employed in (a) and a risk to workers of 3.4×10^{-2} Sv^{-1} year^{-1} (Stather et al, 1988) was used in (b).

Table VI. Average annual occupationally related dose (mSv) for samples of workers for different groups using radiation in hospitals (Hughes et al, 1989)

Group	Diagnostic radiology	Nuclear medicine	Radiotherapy
Radiologists and other clinicians	0.27	0.05	0.44
Radiographers	0.16	1.22	0.18
Darkroom technicians	0.10	—	—
Nurses	0.07	0.62	[a]0.49, [b]0.56
Physicists	0.09	0.31	[c]0.30
Radioisotope technicians	—	0.43	—
Porters and clerks	0.07	—	0.01
All	0.16	0.12	0.41

The radiotherapy nurses comprise [a]theatre nurses, [b]ward nurses and [c]physicists and technicians.

The average annual dose received by the UK workers using radiation is 1.1 mSv and the risk of death is compared with that of other occupations in Table V(b). The doses individual workers receive have declined. In 1987 there were approximately 2000 workers in the UK who exceeded 15 mSv, and they included about 700 fuel processing workers, 550 tin miners and 60 power station employees. Among the users of ionizing radiation in medicine, less than 10 workers out of 40 000 monitored in 1986 exceeded the current recommended limit of 15 mSv year^{-1} (Hughes et al, 1989). The average annual doses for NHS hospital staff in the departments of diagnostic radiology, nuclear medicine and radiotherapy are given in Table VI.

Occupational exposure represents only 0.2% of the annual collective dose to the UK population, whereas medical irradiation (mainly from diagnostic radiology) contributes 12%, which is the major part of man-made sources. It is commonly recognized that the benefits of diagnostic procedures generally outweigh any somatic (non-genetic) effects (Medical Research Council, 1960). There is a large range of doses for different types of radiological examination (Table VII) and, although the frequency of X-ray examinations has increased, the UK average annual "genetically significant dose" to the gonads has slightly decreased since the 1950s to 120 μGy (Darby et al, 1980).

It is not the workplace, but radiation from natural sources that contributes the major share (87%) of the total radiation exposure of the UK population. Radon gas from terrestrial uranium and thorium is the major source of natural radiation. Radon decay products make up about a half (1.3 mSv) of the annual collective

Table VII. The effective dose equivalents for the most frequent radiological and nuclear medicine examinations in NHS hospitals in the UK (Shrimpton et al, 1986; Wall et al, 1985)

Examination	Dose per examination (mSv)		
	Minimum	Mean	Maximum
Radiological (simple):			
Lumbar spine	0.37	2.15	7.37
Chest	<0.01	0.05	1.32
Skull	0.01	0.15	0.50
Abdomen	0.12	1.39	9.94
Thoracic spine	0.16	0.92	4.39
Pelvis	0.09	1.22	5.77
Radiological (complex):			
Intravenous	1.4	4.36	35.05
Barium meal	0.6	3.83	24.39
Barium enema	2.92	7.69	33.64
Cholecystography	0.13	0.95	5.01
Nuclear medicine ($^{99}Tc^m$):			
Bone phosphate compounds scan	2.21	3.48	4.95
Liver colloid scan	0.46	1.13	2.51
Brain pertechnetate scan	3.30	4.90	8.00
Lung MAA/microspheres perfusion	0.46	1.10	2.78
Thyroid pertechnetate scan	0.15	0.75	2.00
Kidney DTPA (chelates) scan	0.37	2.48	5.55

Table VIII. UK lifetime risk estimates (whole population) of premature death from radon (lung cancer) compared with other causes (Wrixon et al, 1988; NRPB, 1990)

Cause	Gas (Bq m^{-3})	Dose (mSv $year^{-1}$)	Life risk (%)
All cancer, all causes	—	—	25
Radon, highest 1% of UK homes	>1000	>50	>15
Lung cancer, all causes	—	—	6
Radon, Action Level	200	10	3
Motor vehicle accidents	—	—	1
Accidents in homes	—	—	1
Pedestrian traffic accidents	—	—	0.3
Radon, UK average	20	1	0.3
Domestic fires	—	—	0.06

Exposure to radon is expressed as effective dose equivalent, and the risk in accordance with the DS86 dosimetry.

effective dose equivalent from all natural sources put together. It was realized comparatively recently that the indoor exposure varies substantially from one dwelling to another (Cliff, 1978), ranging from about 0.3 mSv to over 100 mSv for some residents in south-west England (Table VIII). The induction of lung cancer by alpha-emitting daughter products of radon gas is well documented for uranium miners. Recent studies claim that radon in homes is the second most important cause of lung cancer and could have a synergistic effect when coupled with smoking (BEIR IV, 1988). The magnitude of the cause and effect relationship between radon in domestic dwellings and lung cancer is less certain than for radon in mines (Haynes, 1988). It is generally assumed that domestic radon exhibits a linear, non-threshold (stochastic) response, although a lack of epidemiological evidence has caused Cohen (1990) to challenge this view.

The average UK radon concentration is 20 Bq m^{-3} of inhaled air. The UK Action Level, where remedial action is advised, has been reduced recently from 400 to 200 Bq m^{-3}, corresponding to a dose of 10 mSv $year^{-1}$ with a lifetime risk of lung cancer of 3.0% (O'Riordan et al, 1987; NRPB, 1990). This reduction in the Action Level, owing to revised risk estimates, means that about 75000 instead of 20000 homes are now above the Action Level. The assessment of lifetime risk for the average UK smoker from lifelong radon exposure at an average concentration of 20 Bq m^{-3} approaches 1%, whereas the mean value for non-smokers is 0.1%, compared to a 0.3% risk for the whole population of the UK.

A major part of the dose from radioactivity in the body, internal radiation, is due to potassium-40. Its concentration in the body is metabolically controlled and thus there is a small variation in the average annual dose of 180 μSv from this radionuclide (UNSCEAR, 1988). Other contributions to internal dose arise from the decay products of terrestrial uranium and thorium, and there are differing views on whether ingestion or inhalation is the most dominant (Hill, 1965; Clemente et al, 1979). Radon, thoron and their decay products primarily irradiate the lung, but also contribute to the internal radiation dose. It has been shown that for uranium miners the body burdens of lead-210 and polonium-210 (beta- and alpha-emitting long-lived daughters of uranium-238) are related to their working lifetime, cumulative exposure to radon in the mines (Blanchard et al, 1969). Henshaw et al (1988a) have predicted that the public's internal radiation doses can be expected to have a wider range than realized at present, primarily owing to the variability of domestic radon concentrations.

Increased incidences of childhood leukaemia have been reported in the vicinity of nuclear installations, especially those with relatively high alpha-particle waste, such as Sellafield and Dounreay. However, the causes of these and other "clusters" are far from clear (Dionian et al, 1986; Stather et al, 1986). The few measurements made of body burden alpha radioactivity in the UK are not commensurate with these epidemiological findings (Henshaw et al, 1988b). A hypothesis is that the childhood leukaemia clusters have a genetic origin, with irradiation of parents while working for the nuclear industry (Milne, 1989). Besides studies concerned with radiation, other sources, such as an influx of viral infections from newcomers (Kinlen, 1988), are being investigated as the possible cause of the excess childhood leukaemia around nuclear sites.

Future direction of radiation risk research

For some time, there has been discussion as to whether viruses cause cancer in man. To date, 20% of world, mainly non-western, cancers have been reported to be induced by DNA viruses (Marx, 1989). Carriers of the hepatitis B virus have a much greater risk of getting spontaneous liver cancer than that of non-carriers. The possibility of increased susceptibility to radiation-induced cancer because of viral or other genetic defects is under study (UNSCEAR, 1988). It has been hypothesized that the pattern of occurrence of excess tumours, including the latent period and age-related characteristics, fits a multistage, perhaps two-event, model with radiation as the initiating agent (Moolgavkar & Knudson, 1981). There is strong evidence that the effects of aging and other promoting factors, such as smoking, affect the later stages of stimulating tumour growth (Jacobi, 1988). An improved understanding of the way radiation induces cancers and hereditary defects, such as the activation of viruses in radiation-induced tumours (Schmidt et al, 1988) will influence future concepts on radiation risk and protection.

Recent research has shown that radiation effects to the individual are not only dependent on age and sex. Screening methods are being developed to identify human genotypes that are known to have an increased susceptibility to ionizing radiation. These include patients with the radiosensitive disorder ataxia-telangiectasia (AT). The "at risk" group, AT heterozygotes, is estimated to comprise between 0.5% and 5% of the total population, who exhibit a twofold elevated lifetime risk of fatal neoplasia (Gentner et al, 1988). Bloom's syndrome and Fanconi's anaemia are two other rare congenital diseases in which there is evidence of a defect in DNA management. Children with these congenital diseases have a greater risk of spontaneous and possibly radiation-induced cancers including leukaemia (Margulis, 1985).

Risk analysis of cancer and hereditary defects induced in humans by irradiation has always been a complex matter with many controversial aspects. The present time is no exception. In general, radiation risk estimates have large uncertainties, in particular those for low dose-rate cumulative exposures. There are uncertainties of the harm from exposure *in utero* and of children, especially in estimating the excess carcinomas that normally express themselves in adulthood. Confidence in these groups' risk estimates will improve with increased epidemiological data from longer follow-up periods for the Japanese study and medical irradiations. Radiation can change the time and cause, but not the overall probability of death (Dunster, 1989). Incidence, severity, fatalities and years of lost life are all indices that could influence future radiation dose limits and regulations.

Interim figures for radiation risk estimates and dose limits have been published in the last 2 years by the ICRP and NRPB (ICRP, 1987; NRPB, 1987; Clarke, 1988), following new dosimetry and an extention of the Japanese life span study. A major review by UNSCEAR (1988) has recently been published and another by the US BEIR-5 Committee is expected soon. These will then be used by the ICRP, who are reviewing risk, organ weighting factors and dose limits. The ICRP's recommendations are due in 1990, and hopefully will stabilize national debate with international consensus.

Acknowledgments

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References

BEIR III, 1980. The effects on populations of exposure to low levels of ionizing radiation (National Academy Press, Washington).

BEIR IV, 1988. Health risks of radon and other internally deposited alpha-emitters (National Academy Press, Washington).

BENINSON, D. & SOWBY, F. D., 1985. Age and sex dependent weighting factors for medical irradiation. *Radiation Protection Dosimetry, 11*, 57–60.

BLANCHARD, R. L., ARCHER, V. E. & SACCOMANNO, G., 1969. Blood and skeleton levels of ^{210}Pb–^{210}Po as a measure of exposure to inhaled radon daughter products. *Health Physics, 16*, 585–596.

BOICE, J. D., DAY, N. E., ANDERSON, A., ET AL, 1985. Second cancers following radiation treatment for cervical cancer. An international collaboration among cancer registries. *Journal of the National Cancer Institute, 74*, 955–975.

CLARKE, R. H., 1988. *Statement of Evidence to the Hinkley Point C Inquiry*, (*NRPB-M160*) (Her Majesty's Stationery Office, London).

CLARKE, R. H. & SOUTHWOOD, T. R. E., 1989. Risks from ionizing radiation. *Nature, 338*, 197–198.

CLEMENTE, G. F., RENZETTI, A. & SANTORI, G., 1979. Assessment and significance of the skeletal doses due to ^{210}Po in radon spa workers. *Environmental Research, 18*, 120–126.

CLIFF, K. D., 1978. Assessment of airborne radon daughter concentrations on dwellings. *Physics in Medicine and Biology, 23*, 696–711.

COHEN, B. L., 1990. An experimental test of the linear no threshold theory of radiation carcinogenesis. *Environmental Research* (in press).

DARBY, S. C., 1986. Epidemiological evaluation of radiation risk using population exposed at high doses. *Health Physics, 51*, 269–281.

Darby, S. C., Kendall, G. M., Rae, S. & Wall, B. F., 1980. *The Genetically Significant Dose from Diagnostic Radiology in Great Britain in 1977* (*NRPB-R106*) (Her Majesty's Stationery Office, London).

Darby, S. C., Doll, R., Gill, S. K. & Smith, P. G., 1987. Long term mortality after a single treatment course with X-rays in patients treated for ankylosing spondylitis. *British Journal of Cancer, 55,* 179–190.

Dionian, J., Muirhead, C. R., Wan, S. L. & Wrixon, A. D., 1986. *The Risks of Leukaemia and Other Cancers in Thurso from Radiation Exposure,* (*NRPB-R196*) (Her Majesty's Stationery Office, London).

Dunster, H. J., 1989. Setting radiation standards. *Nature, 337,* 311.

Fleischmann, A. B. & Webb, G. A. M., 1986. Valuations of health detriment on the optimisation of radiological protection: a current NRPB view. In *Proceedings of International Symposium on Optimisation of Radiation Protection, Vienna* (IAEA, Vienna) 487–498.

Fry, T. J. M., Storer, J. B. & Burns, F. J., 1986. Radiation induction of cancer of the skin. In *Radiation Damage to Skin (British Journal of Radiology Supplement 19),* ed. by H. Jammet et al (BIR, London), pp. 58–60.

Gentner, N. E., Morrison, D. P. & Myers, D. K., 1988. Impact of radiogenic cancer risk of persons exhibiting abnormal sensitivity to radiation. *Health Physics, 55,* 412–425.

Haynes, R. M., 1988. The distribution of domestic radon concentrations and lung cancer mortality in England and Wales. *Radiation Protection Dosimetry, 25,* 93–96.

Health and Safety Executive, 1988. *The Tolerability of Risk from Nuclear Power Stations* (Her Majesty's Stationery Office, London).

Henshaw, D. L., Hatzialekou, U. & Randle, P. H., 1988a. Analysis of alpha-particle autoradiographs of bone samples from adults and children in the UK at natural levels of exposure. *Radiation Protection Dosimetry, 22,* 231–242.

Henshaw, D. L., Richardson, R. B., Allen, J. E. & Randle, P. H., 1988b. *Fetal Transfer of Alpha-radionuclides in the Human Population at Natural Levels of Exposure* (EULEP, Harwell).

Hill, C. R., 1965. Polonium-210 in man. *Nature, 208,* 423–428.

Hughes, J. S., Shaw, K. B. & O'Riordan, M. C., 1989. *Radiation Exposure of the UK Population—1988 Review (NRPB-R227)* (Her Majesty's Stationery Office, London).

Ichimaru, R. & Ishimaru, T., 1975. Leukaemia and related disorders. *Journal of Radiation Research (Japan), 16: Suppl.,* 89–96.

ICRP, 1977. *Publication 26, Recommendations of the Commission* (Pergamon Press, Oxford).

—— 1977. *Publication 27, Problems Involved in Developing an Index of Harm* (Pergamon Press, Oxford).

—— 1985. *Publication 45, Quantitative Basis for Developing a Unified Index of Harm* (Pergamon Press, Oxford).

—— 1985. *Statement from the 1985 Paris meeting of the ICRP, Vol. 15, No.3* (Annals of the ICRP).

—— 1987. *Statement from the 1987 Como Meeting of the ICRP, Radiological Protection Bulletin, No. 86 Supplement.*

Ionizing Radiations Regulations, 1985. *SI 1333* (Her Majesty's Stationery Office, London).

Jacobi, W., 1988. Environmental radioactivity and man—the 1988 Sievert lecture. *Health Physics, 55,* 845–853.

Kinlen, L., 1988. Evidence for an infective cause of childhood leukaemia: comparison of a Scottish new town with nuclear reprocessing sites in Britain. *Lancet, ii,* 1323–1327.

Little, M. P. & Charles, M. W., 1989. Estimation of population cancer risks from the DS86 bomb survivor data. *Journal of Radiological Protection, 9,* 9–18.

Margulis, A. R., 1985. The effects of low-dose radiation: research still needed. *American Journal of Roentgenology, 145,* 431–432.

Marx, J. L., 1989. How DNA viruses may cause cancer. *Science, 243,* 1012–1013.

Mays, C. W., 1988. Stochastic and nonstochastic concepts: is revision needed? *Health Physics, 55,* 437–441.

Medical Research Council, 1956. *The Hazards to Man of Nuclear and Allied Radiations* (Her Majesty's Stationery Office, London).

Medical Research Council, 1960. *The Hazards to Man of Nuclear and Allied Radiation. A Second Report* (Her Majesty's Stationery Office, London).

Milne, A., 1989. Leukaemia clusters may have genetic origin. *New Scientist,* (17th June) 39.

Mole, R. H., 1974. Antenatal irradiation and childhood cancer. Causation or coincidence. *British Journal of Cancer, 30,* 199–208.

Mole, R. H., 1987. Irradiation of the embryo and fetus. *British Journal of Radiology, 60,* 17–31.

Monson, R. R. & MacMahon, B., 1984. Prenatal X-ray exposure and cancer in children. In *Radiation Carcinogenesis: Epidemiology and Biological Significance,* ed. by J. D. Boice & J. F. Fraumeri, Jr. (Raven Press, New York).

Moolgavkar, S. H. & Knudson, A. G., 1981. Mutation and cancer: a model for human carcinogenesis. *Journal of the National Cancer Institute, 66,* 1037–1052.

NRPB, ASP9, 1986. *Cost–Benefit Analysis in the Optimisation of Radiological Protection* (Her Majesty's Stationery Office, London).

NRPB, 1987. *Interim Guidance on the Implications of Recent Revisions of Risk Estimates and the ICRP 1987 Como Statement (NRPB-GS9)* (Her Majesty's Stationery Office, London).

NRPB, 1990. *Limitation of human exposure to radon in homes. Documents of the NRPB, Vol. 1, No. 1* (HMSO, London).

OPCS, 1981. *Cancer Statistics: Incidence, Survival and Mortality in England and Wales. Studies on Medical and Population Subjects, No. 43* (Her Majesty's Stationery Office, London).

O'Riordan, M. C., James, A. C., Green, B. M. R. & Wrixon, A. D., 1987. *Exposure to Radon Daughters in Dwellings (NRPB-GS6)* (Her Majesty's Stationery Office, London).

Otake, M. & Schull, W. J., 1984. In utero exposure to A-bomb radiation and mental retardation: a reassessment. *British Journal of Radiology, 57,* 409–414.

Otake, M., Yoshimaru, H. & Schull, W. J., 1988. *Severe Mental Retardation among Prenatally Exposed Survivors of the Atomic Bombing of Hiroshima and Nagasaki: A Comparison of the T65DR and DS86 Dosimetry Systems (RERF TR16–87)* (Radiation Effects Research Foundation, Hiroshima).

Pochin, E. E., 1980. The need to estimate risks. *Physics in Medicine and Biology, 25,* 1–12.

Preston, D. C. & Pierce, E. A., 1987. *The Effects of Changes in Dosimetry on Cancer Mortality Risk Estimates in the Atomic Bomb Survivors (RERF 9–87)* (Radiation Effects Research Foundation, Hiroshima).

Ron, E., Modan B. & Boice, J. D., 1988. Mortality after radiotherapy for ringworm of the scalp. *American Journal of Epidemiology, 127,* 55–64.

Russell, J. G. B., 1986. Assessment of priorities when introducing some radiation protection methods in radiodiagnosis. *British Journal of Radiology, 59,* 153–156.

Schmidt, J., Luz, A. & Erfle, V., 1988. Endogenous marine leukaemia viruses frequency of radiation-activation and novel effects of viral isolates. *Leukaemia Research, 12,* 393–403.

Shimizu, Y., Kato, H., Schull, W. J., Preston, D. L., Fujita, S. & Pierce, D. A., 1987. *Life Span Study Report 11, Part I: Comparison of Risk Coefficients for Site-Specific Cancer Mortality Based on DS86 and T65DR Shielded Kerma and Organ Doses (RERF TR12–87)* (Radiation Effect Research Foundation, Hiroshima).

Shimizu, Y., Kato, H. & Schull, W. J., 1988. *Life Span Study Report 11, Part II: Cancer Mortality in the Years 1950–1985 Based on the Recently Revised Doses (DS86) (RERF TR5–88)* (Radiation Effects Research Foundation, Hiroshima).

Shrimpton, P. C. & Wall, B. F., 1986. *Doses to Patients from Medical Radiological Examinations in Great Britain (Radiological Protection Bulletin, No. 77)* (NRPB, Chilton).

Smith, P. G. & Doll, R., 1981. Mortality from cancer and all causes among British radiologists. *British Journal of Radiology, 54,* 187–194.

Stather, J. W., Dionian, J., Brown, J., Fell, T. P. & Muirhead, C. R., 1986. *The Risks of Leukaemia and Other Cancers in Seascale from Radiation Exposure (NRPB-R171, Addendum)* (Her Majesty's Stationery Office, London).

Stather, J. W., Muirhead, C. R., Edwards, A. A., Harrison, J. D. & Wood, N. R., 1988. *Health Models Developed from the 1988 UNSCEAR Report NRPB-R226* (Her Majesty's Stationery Office, London).

Stewart, A. M. & Kneale, G. W., 1970. Radiation dose effects in relation to obstetric X-rays and childhood cancers, *Lancet, i,* 1185–1188.

The Royal Society, 1983. *Risk Assessment—A Study Group Report* (London).

UNSCEAR, 1977. *Sources and Effects of Ionizing Radiations* (United Nations, New York).

—— 1986. *Genetic and Somatic Effects of Ionizing Radiation* (United Nations, New York).

—— 1988. *Sources, Effects and Risks of Ionizing Radiation* (United Nations, New York).

Wall, B. F., Hillier, M. C. & Kendall, G. M., 1985. Nuclear medicine activity in the United Kingdom. *British Journal of Radiology, 58,* 125–130.

Wrixon, A. B., Green, B. M. R., Lomas, P. R., et al, 1988. *Natural Radiation Exposure in UK Dwellings (NRPB-R190)* (Her Majesty's Stationery Office, London).

Yoshimoto, Y., Kato, H. & Schull, W. J., 1988. Risk of cancer among children exposed in utero to A-bomb radiations, 1950–84. *Lancet, ii,* 665–669.

Bibliography

This is a list, with comments, of recent books on radiation and risks, in alphabetical order by author.

(1) *Living with Risk.* By the British Medical Association, pp. 280, 1987 (Wiley, UK), £14.95.
ISBN 0–471–91598X

A softback book, well illustrated and written in a conversational style to its declared aim to improve the public and healthcare workers' risk education. It puts in perspective all aspects of personal risk with radiation being one of them.

(2) *Radiation and Health: The Biological Effects of Low Level Exposure to Ionizing Radiation.* By Robin Russell Jones and Richard Southwood, pp. 292, 1987 (Wiley, Chichester), £19.95.
ISBN 0–471–91674–9

This hardback book contains the edited proceedings of a conference under the auspices of the NRPB and Friends of the Earth. Different scientific viewpoints are refreshingly reflected by antagonists eminent in the fields of radiology, epidemiolgy and environmental medicine.

(3) *Living with Radiation.* By the National Radiological Protection Board, pp. 62, 1989 (NRPB, UK), 4th edn., £3.50.
ISBN 0–85951–3203

This booklet is aimed at a wide readership. It introduces with clarity the nature of ionizing radiations, its sources and effects, and the means of protecting against it. Chapters on nuclear reactors and radioactive waste are included.

(4) *Radiation Risks: an Evaluation.* By David Sumner, pp. 198, 1987 (Tarragon Press, Glasgow), £4.95.
ISBN 1–870781–00–9 (New edition imminent.)

A softback book with chapters on basic radiation physics and radiology through to the nature of radiation risks, including those of the Chernobyl accident. Its comprehensive use of technical terms and references makes it an excellent book for interested students and professionals.

(5) *Radiation, Doses, Effects, Risks.* By United Nations Environment Programme, pp. 64, 1986 (UN Publication No. E.86.III.D.4), £10.
ISBN 92–807–1104–0

This booklet is largely based on earlier UNSCEAR reports but aimed at a broader audience. Its use of good, clear, illustrations and level of technical language makes it accessible to the general educated reader.

Note added in proof

A recent report by Gardner et al (1990) linking childhood leukaemias with the fathers' occupational exposure to radiation at Sellafield may influence future ICRP estimates for hereditary effects and recommended dose limits.

Reference

Gardner, M. J., Snee, M. P., Hall, A. J., Powell, C. A., Downes, S. & Terrell, J. D., 1990. Results of case-control study of leukaemia and lymphona among young people near Sellafield nuclear plant in West Cumbria. *British Medical Journal, 300,* 423–429.

1990, *The British Journal of Radiology*, *63*, 246–250

Ultrasound evaluation of ectopic pregnancy including correlation with human chorionic gonadotrophin levels

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Abstract. A total of 267 patients referred for ultrasound examination because of clinical suspicion of ectopic pregnancy were studied prospectively. The outcome was correlated with the ultrasound findings and human chorionic gonadotrophin levels using a quantitative serum assay. The value of the following in the diagnosis of ectopic pregnancy are assessed: ultrasound criteria for early diagnosis of intrauterine pregnancy before visualization of a viable fetus, the discriminatory zone of hCG and extrauterine abnormalities.

Ectopic pregnancy is a serious condition. It accounts for 10% of maternal deaths and recent reports have emphasized that its incidence is increasing (Cole & Clarke, 1988; Flett et al, 1988; Newton, 1988). Clinical diagnosis is correct in less than 50% of cases (Weckstein, 1985). The symptoms and signs are similar to those of many other gynaecological disorders and clinical suspicion will be high in any woman of child-bearing age who presents with lower abdominal pain and abnormal vaginal bleeding. Weinsten et al (1983), in a review of 154 patients with an ectopic pregnancy, reported that only 61% of patients claimed a "missed period". Ectopic pregnancy is suspected by clinicians 10 times more often than it occurs (Kadar et al, 1981) and radiology departments providing an ultrasound service for gynaecological patients will receive many referrals for a suspected ectopic pregnancy. It is important therefore that the strengths and limitations of ultrasound examination and the interrelation between ultrasound and biochemical pregnancy tests are known. Early reports suggest that the diagnostic accuracy of ultrasound may be greater using transvaginal probes (Nyberg et al, 1987). However, these are not yet in widespread use and this report is based on abdominal scanning.

When examining a patient with a suspected ectopic pregnancy the ultrasonographer is faced with a series of questions. Is there evidence of an intrauterine pregnancy? Is there a viable fetus? If there is an empty fluid collection in the uterus, does it represent a true gestational sac (Fig. 1) or the decidual cast of an ectopic pregnancy (Fig. 2)? Is the uterus apparently empty? Can the ectopic pregnancy be positively identified in the adnexal regions?

The pseudogestational sac of an ectopic pregnancy (Marks et al, 1979) may be mistaken for a true gestational sac and lead to the erroneous diagnosis of intrauterine pregnancy. Bradley et al (1983) described the double decidual sign of the true gestational sac. Abramovici et al (1983) stressed that true gestational sacs are eccentrically placed in the uterus, whereas the pseudogestational sac is central because it represents fluid in the cavity. Both concepts may help to differentiate between a true gestational sac and a pseudogestational sac.

An apparently empty uterus on ultrasound examination may indicate the absence of pregnancy, an ectopic pregnancy, an intrauterine gestation of less than 5 weeks menstrual age or a recent abortion. Modern assays of human chorionic gonadotrophin (hCG) are highly sensitive and will reliably diagnose pregnancy even in ectopic gestations, which tend to produce lower levels. It is

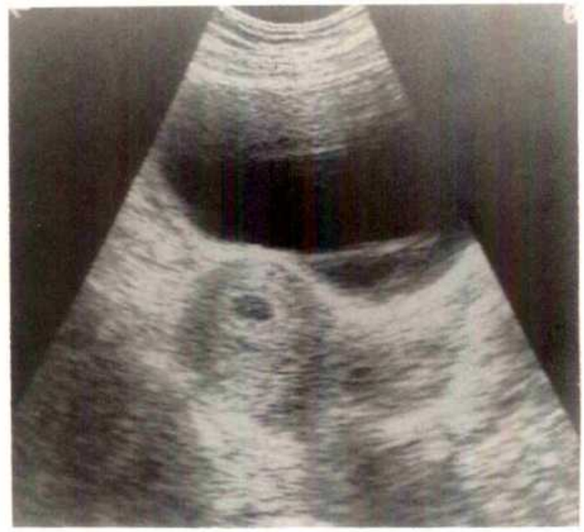

Figure 1. Longitudinal section of the uterus showing an empty gestational sac at 6 weeks amenorrhoea.

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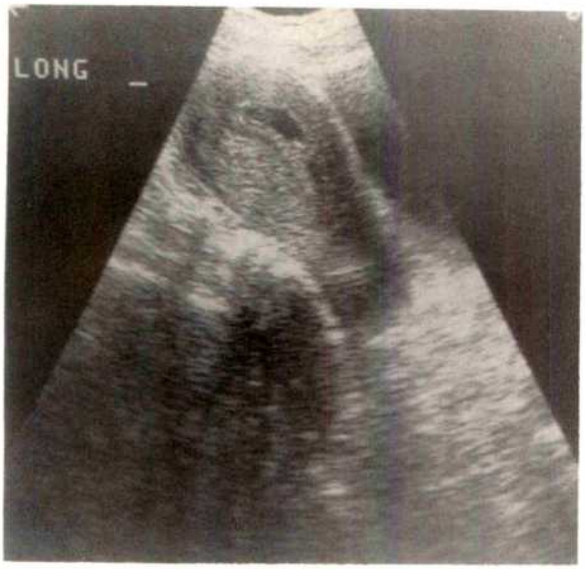

Figure 2. Longitudinal section of the uterus showing a "pseudo gestational sac" in ectopic pregnancy.

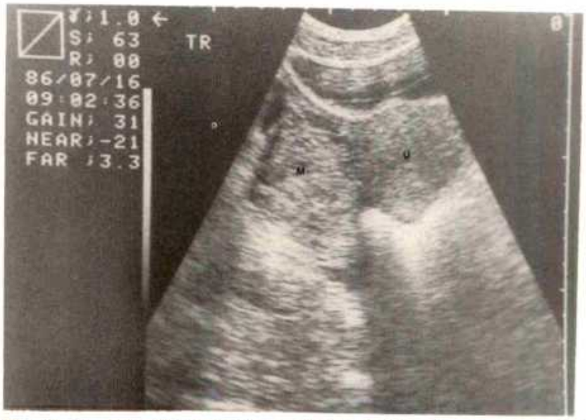

Figure 3. Transverse section of the pelvis showing a solid adnexal mass (M) and the uterus (U).

possible to detect hCG on average 9 days after ovulation in serum and after 13 days in urine. Using abdominal ultrasound, a gestational sac is not visible until 3 weeks post-conception. This may give rise to the problem of biochemical evidence of pregnancy and an apparently empty uterus on ultrasound. Kadar et al (1981) evolved the concept of the discriminatory zone of hCG (the serum level at which a gestational sac will be visualized in normal pregnancy) to help solve this problem.

The value of adnexal findings in the diagnosis of ectopic pregnancy has been questioned, since the appearances are often non-specific.

Method

The 267 consecutive patients referred for clinical suspicion of an ectopic pregnancy were examined using convex linear realtime ultrasound equipment (Picker LS 7000). Uterine contents were classified as empty (no gestational sac), empty gestational sac (sac with double echogenic rim, eccentrically placed), gestational sac with viable fetus, or other uterine fluid collection (centrally placed, no echogenic rim). Adnexal masses were classified as solid or complex (Fig. 3) or cystic (Fig. 4). Note was made of fluid (transonic) or haematoma (material with low level echoes or of mixed echoity) in the pelvic cavity.

Serum hCG assays were performed using an immunoradiometric assay (Maiaclone, Serono, calibrated against the first International Reference Population, IRP). The hCG assays were performed within 24 h of the ultrasound scan and scans were performed without knowledge of the hCG levels. Outcome variables were

(i) ectopic pregnancy (surgically diagnosed),
(ii) viable intrauterine pregnancy (finding of a viable fetus on subsequent ultrasound examinations),
(iii) non-viable intrauterine pregnancy (no viable fetus on ultrasound and the pregnancy ending in spontaneous abortion or uterine evacuation, including anembryonic pregnancy, missed abortion, inevitable, incomplete and complete abortion) and
(iv) patients with no pregnancy (hCG levels below 3 miu/ml).

Because of differences in hCG assays, a local discriminatory zone was determined by review of the hCG levels in patients with intrauterine gestation sacs in whom subsequent progress indicated a viable pregnancy. A level of 4000 miu/ml (1st IRP) was considered appropriate (Fig. 5), similar to that of other workers (Filly, 1987). The lowest level at which a gestational sac was identified was 2740 miu/ml, although sacs were not consistently visualized at this level.

Results

Of the patients, 132 (49%) were pregnant, 53 (20%) had an ectopic pregnancy and 79 (29%) had an intrauterine pregnancy; 135 (51%) were not pregnant (see Table I).

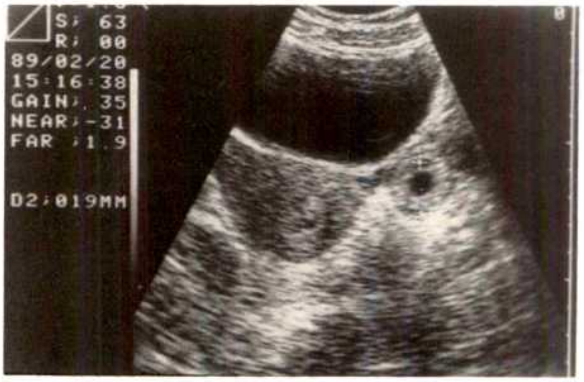

Figure 4. Transverse section of the pelvis showing a 19 mm thick walled cystic lesion (the ectopic gestation) and a small fluid collection in the uterus.

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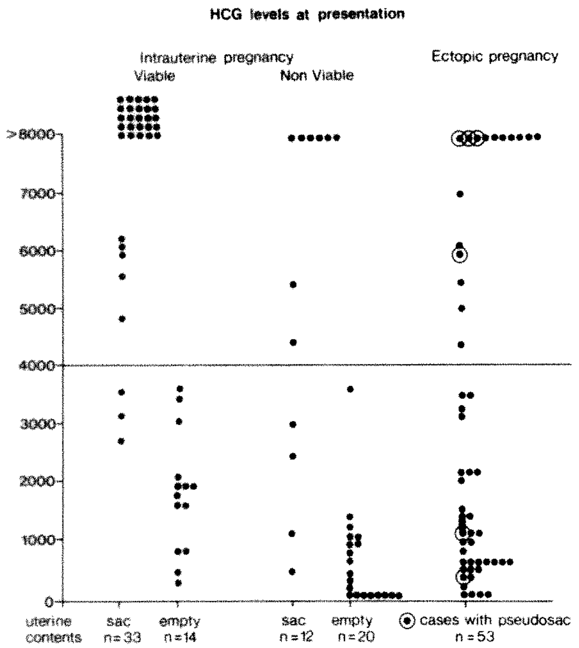

Figure 5. The hCG levels of 267 patients at initial presentation. Patients are subdivided into intrauterine pregnancies: viable (sac in uterus, empty uterus), non-viable (sac in uterus, empty uterus) and ectopic pregnancy. The hCG levels on the vertical axis are in miu/l. The horizontal line at 4000 miu/l marks the local discriminatory zone.

Table I. Final diagnosis of 267 patients

Pregnant	132	(49%)
Ectopic	53	(20%)
Intrauterine	79	(29%)
Viable	47	
Non-viable	32	
Non-pregnant	135	(51%)
Ovarian cysts	10	
Appendicitis	1	
Pelvic inflammatory disease/undiagnosed abdominal pain	124	

Table II. Diagnostic indices for discriminatory zone of hCG in the diagnosis of ectopic pregnancy

Sensitivity	25%
Specificity	100%
Positive predictive value	100%
Negative predictive value	49%

Note.
Positive test: hCG > 4000 miu/ml with empty uterus
Negative test: hCG < 4000 miu/ml with empty uterus

Intrauterine contents—uterus containing an empty fluid collection—differentiation between a true gestational sac and pseudosac

Fifty-one patients with biochemical evidence of pregnancy had an empty fluid collection in the uterus.

Forty-five patients were subsequently shown to have an intrauterine pregnancy (33 viable, 12 non-viable) and these were all correctly diagnosed by ultrasound. There were three negative laparoscopies in this group where the clinical presentation cast doubt on the ultrasound diagnosis of intrauterine pregnancy.

Six patients were subsequently shown to have an ectopic pregnancy and the ultrasound appearances caused confusion in five of these. In three the appearances were equivocal and an intrauterine pregnancy could not be excluded, and in two the fluid collections were misinterpreted as a collapsed gestational sac in patients who were first referred to the department as threatened abortions. Diagnostic laparoscopy was delayed in the last two cases.

Intrauterine contents—the empty uterus—the discriminatory zone of hCG

The levels of hCG at presentation are given in Fig. 5.

Twelve patients had an hCG greater than 4000 miu/ml and an empty uterus on ultrasound. All were subsequently shown to have an ectopic pregnancy.

Sixty-nine patients had an hCG below 4000 miu/ml and an empty uterus on ultrasound. Of these, 35 were subsequently shown to have an ectopic pregnancy and 34 an intrauterine pregnancy (14 viable, 20 non-viable). Twelve negative laparoscopies were performed in the group on patients subsequently shown to have an intrauterine pregnancy.

Diagnostic indices are given in Table II.

Extrauterine findings—adnexal masses and free fluid

The extrauterine findings for the groups of patients with an ectopic pregnancy, those with an intrauterine pregnancy and non-pregnant patients are given in Table III.

There was a much higher incidence of abnormal adnexal findings in the patients with an ectopic preg-

Table III. The extrauterine findings for 267 patients

	None	Adnexal solid/complex mass	Cystic adnexal mass	Fluid only	Complex + fluid	Cystic + fluid
Ectopic pregnancies ($n = 53$)	7 (13%)	20 (38%) (2 ectopic fetuses)	12 (23%)	14 (26%)	12 (23%)	17 (32%)
Intrauterine pregnancy ($n = 79$)	62 (79%)	1 (1%)	12 (15%)	4 (5%)	—	—
Non-pregnant ($n = 135$)	84 (63%)	10 (7%)	32 (24%)	9 (6%)	4 (3%)	2 (1.5%)

Table IV. The diagnostic indices for extrauterine findings in the 132 patients with biochemical evidence of pregnancy

Diagnostic index	Solid/complex adnexal mass (%)	Cystic adnexal mass (%)	Fluid only (%)	Solid/complex mass+fluid (%)	Cystic mass +fluid (%)
Sensitivity	38	23	26	23	32
Specificity	99	48	95	100	100
Positive predictive value	95	50	77	100	100
Negative predictive value	70	63	66	66	69

nancy than in those with an intrauterine pregnancy or those with no pregnancy.

Of those with an ectopic pregnancy, seven (13%) had no adnexal mass and no free fluid (in conjunction with an empty uterus), *i.e.* a normal ultrasound scan.

A live fetus in an ectopic sac was visible in one case on the initial scan and in a further case, in which there was delay in diagnosis; this finding was present on a second examination.

Twelve (22%) patients with an ectopic pregnancy had a cystic adnexal lesion and in seven of these there was a thick-walled cystic lesion with an echogenic rim suggestive of an ectopic gestational sac. Diagnostic indices for adnexal findings in the diagnosis of ectopic pregnancy (in the group of patients with biochemically proven pregnancy and clinical suspicion of ectopic pregnancy) are given in Table IV.

Discussion

Only 49% of the patients in this study were pregnant. This reflects a high degree of clinical suspicion and a liberal referral policy in our department. The yield in patients who were not pregnant was relatively low: 63% had normal ultrasound examinations. In 10 cases, the final clinical diagnoses were complications of ovarian cysts; there was one case of appendicitis and the remainder were diagnosed as having either pelvic inflammatory disease or abdominal pain of unexplained origin.

Assessment of the uterine contents is central to the ultrasound examination of patients with a suspected ectopic pregnancy. In a patient who has not had assisted reproduction, an intrauterine pregnancy, for practical purposes, excludes an ectopic pregnancy. In spontaneously occurring pregnancies there may be coexistent ectopic and intrauterine gestations in 1:30 000 cases. In induced pregnancies the incidence is much higher. An intrauterine gestation sac with a live fetus is positive proof of an intrauterine pregnancy, but in the majority of patients the gestational age will only be 5–6 weeks and the sac will be empty. Differentiation between a true gestation sac and a pseudosac may be difficult. In this series, 11% of patients with an ectopic pregnancy had a pseudosac. Using the criteria of a double decidual sign and eccentric placement of the sac we were able to identify intrauterine pregnancies correctly. However, in five of the six cases of an ectopic pregnancy with a pseudogestational sac the appearances caused diagnostic confusion, indicating the difficulty in making the positive diagnosis of a pseudosac. In two cases there was mistaken ultrasound diagnosis of an incomplete abortion in patients with an ectopic pregnancy who had first presented with a clinical diagnosis of threatened abortion. In both cases histological examination of products after evacuation of the uterus showed no evidence of chorionic villi, and therefore diagnostic laparoscopy was performed. These cases illustrate the clinical difficulty in making the diagnosis and the importance of considering the diagnosis of ectopic pregnancy in all cases of early pregnancy failure, not just those that present for ultrasound examination because of a clinical suspicion of an ectopic pregnancy.

Kadar et al (1981) defined the discriminatory zone of serum hCG to help assessment of patients with biochemical evidence of pregnancy and an apparently empty uterus on ultrasound. Depending on what type of assay is used, there may be a period of between 1 and 2 weeks when the uterus is apparently empty on ultrasound, despite the presence of an intrauterine pregnancy. The issue is further confused because menstrual history is often unreliable in these patients and the date of ovulation is not known. However, the discriminatory zone is only of value in a small proportion of patients. Ectopic pregnancies produce lower levels of hCG than normal intrauterine pregnancies and, in this series, only 23% of ectopic pregnancies had an hCG above 4000 miu/ml and an empty uterus on ultrasound. The majority of patients (in this study, 52% of those with biochemical evidence of pregnancy) fell in the grey area where the uterus was apparently empty on ultrasound and the hCG below 4000 miu/ml. Of these, roughly equal numbers had ectopic and intrauterine pregnancies. Management of these patients may either be conservative with serial hCG and repeat ultrasound or be diagnostic laparoscopy. In our study, 12 patients in this category had negative laparoscopy. Transvaginal ultrasound may allow earlier definition of intrauterine sacs and limit inappropriate surgery in this group.

The aim of examining the adnexal regions is the positive identification of the ectopic gestation. The presence of a live ectopic embryo is seen in relatively few cases (two in this series). Other findings depend on how advanced the ectopic gestation is and whether it has ruptured and caused bleeding. Adnexal findings are likely to be of most value when the hCG is below 4000 miu/ml and the uterus is empty, or when uterine findings are equivocal. Where only qualitative hCG assays are available, adnexal findings will be of value in all cases. In this situation the finding of a complex mass or cystic mass with thick wall, suggesting an ectopic gestation (Coleman et al, 1985), with or without fluid will provide evidence suggestive of ectopic pregnancy.

In this study the finding of a complex or solid mass had the greatest sensitivity (38%), and the positive predictive values of a solid or complex mass, solid complex mass with fluid and cystic mass with fluid were all high: 95%, 100% and 100%, respectively. They were thus valuable in the identification of ectopic pregnancies but less so in the exclusion of this disease with negative predictive values: 70%, 66% and 69%, respectively.

It is noteworthy that 13% of patients with an ectopic pregnancy had an entirely normal scan, emphasizing that normal ultrasound findings should not lull the clinician into a false sense of security. Again transvaginal ultrasound may allow more accurate identification of the ectopic pregnancy.

In conclusion, the diagnosis of ectopic pregnancy is made after consideration of clinical, biochemical and ultrasound data. Intrauterine pregnancy may be reliably diagnosed in the presence of an empty gestational sac but ultrasonographers must be aware of the dangers of confusing a pseudogestational sac with a true gestational sac. In patients with biochemical evidence of pregnancy and an empty uterus on ultrasound, quantitative assessment of the hCG and the use of a discriminatory zone is of value but this is limited because of the lower levels of hormone production by ectopic pregnancies. Adnexal findings are valuable in the diagnosis of ectopic pregnancy, especially in patients with an apparently empty uterus on ultrasound or where uterine findings are equivocal.

References

ABRAMOVICI, H., AUSLENDER, R., LEWIN, A. & FAKTOR, J. H., 1983. Gestational–pseudogestational sac: a new ultrasonic criteria for differential diagnosis. *American Journal of Obstetrics and Gynaecology, 145*, 377–379.

BRADLEY, W. G., FISKE, C. E. & FILLY, R. A., 1983. The double sac sign of early intrauterine pregnancy: use in exclusion of ectopic pregnancy. *Radiology, 143*, 223–226.

COLE, S. & CLARKE, J. A., 1988. Ectopic pregnancy. *British Medical Journal, 297*, 1046.

COLEMAN, B. G., BARON, R. L., ARGER, P. H., ARENSON, R. L., AXEL, L., MAYER, D. P. & COSTELLO, P., 1985. Ectopic embryo detection using real-time sonography. *Journal of Clinical Ultrasound, 13*, 545–554.

FLETT, G. M. M., URQUHART, D. R., FRASER, C., TERRY, P. B. & FLEMING, J. C., 1988. Ectopic pregnancy in Aberdeen 1950–1985. *British Journal of Obstetrics and Gynaecology, 95*, 740–746.

FILLY, R. A., 1987. Ectopic pregnancy: the role of sonography. *Radiology, 162*, 661–668.

KADAR, N., CALDWELL, B. V. & ROMERO, R., 1981. A method of screening for ectopic pregnancy and its indications. *Obstetrics and Gynaecology, 58*, 162–165.

KADAR, N., DEVORE, G. & ROMERO, R., 1981. Discriminatory hCG zone: its use in the sonographic evaluation for ectopic pregnancy. *Obstetrics and Gynaecology, 58*, 156–161.

MARKS, W. N., FILLY, R. A., CALLEN, P. W. & LAING, F. C., 1979. The decidual cast of ectopic pregnancy: a confusing ultrasonographic appearance. *Radiology, 133*, 451–454.

NEWTON, J., 1988. Ectopic pregnancy. *British Medical Journal, 297*, 633–634.

NYBERG, D. A., MACK, L. A., JEFFERY, R. B. & LAING, F. C., 1987. Endovaginal sonographic evaluation of ectopic pregnancy: a prospective study. *American Journal of Roentgenology, 149*, 1181–1186.

WECKSTEIN, L. N., 1985. Current perspective on ectopic pregnancy. *Obstetrical and Gynaecological Survey, 40*, 259–272.

WEINSTEN, L., MORRIS, M. B., DOTTERS, D. & CHRISTIAN, C. D., 1983. Ectopic pregnancy—a new surgical epidemic. *Obstetrics and Gynaecology, 61*, 698–701.

1990, *The British Journal of Radiology*, *63*, 251–256

The role of the STIR sequence in magnetic resonance imaging examination of bone tumours

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Abstract. Sixty patients with primary bone tumours were evaluated with magnetic resonance imaging (MRI) at 0.5 T with both conventional spin–echo (SE) and short inversion time inversion recovery (STIR) sequences. The results have been reviewed in order to evaluate the accuracy of STIR and conventional SE sequences in the detection of tumours, the definition of intramedullary extent and soft-tissue involvement. The intraosseous neoplastic extent has been compared with macroslides of surgical specimens in 24 cases. The role of the STIR sequence in detection of recurrences in the post-surgical follow-up was also evaluated. The STIR sequence, designed to suppress signal from fat, also enhances the signal from tissue with long T_1 and T_2 relaxation times, such as neoplastic and inflammatory tissue. The STIR sequence with T_1 of 120–130 ms in all cases suppressed the high signal from fatty bone marrow, giving a clear depiction of tumour extent, in both its intramedullary and soft-tissue components, and is superior to conventional SE images. The high sensitivity (100% of our cases) of this technique is counterbalanced by its lack of specificity: on STIR sequences both tumour and peritumorous oedema give an increase of signal intensity, limiting assessment of tumour extent. Peritumoral oedema, only present in our series in malignant neoplasms, may however be differentiated on the basis of the configuration of the abnormal areas, and by comparing STIR images with short repetition time/echo time sequence results.

The impact of magnetic resonance imaging (MRI) in the evaluation of musculoskeletal neoplasms has greatly enhanced detection and delineation of bone tumours compared with conventional modalities, such as plain radiography, computed tomography (CT) or scintigraphic techniques (Zimmer et al, 1985; Berquist, 1987; Richardson et al, 1986).

For limb-salvage local resection, there is a need for the assessment of tumour extent within the bone, the detection of skip metastases, the determination of soft tissue and subperiosteal components and the delineation of intra-articular extension. Pre-operative MRI can provide this information (Sundaram et al, 1986). At present, conventional radiography and CT are more specific than MRI in assessing the biological activity, the differential diagnosis of bone tumours and tumour-like lesions and in identifying the typical hallmarks of different tumours (Zimmer et al, 1985; Richardson et al, 1986; Pettersson et al, 1987; Sartoris & Resnick, 1987; Haggar & Froelich, 1988). The lack of specificity of MRI spin–echo (SE) sequences in identifying skeletal neoplasms, on the basis of their usually lengthened relaxation parameters, has been consistently demonstrated (Zimmer et al, 1985, 1986; Daffner et al, 1986; Beltran et al, 1987; Boyko et al, 1987; Petterson et al, 1987, 1988).

For the high contrast provided between the low signal intensity (SI) of tumours and the hyperintensity of bone marrow, the short TR/TE sequence (*i.e.* T_1-weighted) has become the technique of choice in defining intramedullary tumour extent. The high accuracy of this pulse sequence in measuring the medullary bone involvement has been reported (Gillespy et al, 1988). However, in assessing soft-tissue extent, because of the similar SI between tumour and muscle planes, the short repetition time (TR)/echo time (TE) sequence is less reliable.

On long TR/TE (*i.e.* T_2-weighted) images, most neoplasms, because of their long T_2 relaxation times, show an increase in SI approaching that of bone marrow, and only a minimal contrast between them is obtained. However, long TR/TE studies provide excellent details of extraosseous spread because of a higher contrast at tumour soft-tissue interfaces (Zimmer et al, 1985, 1986; Sundaram et al, 1986; Petterson et al, 1987, 1988; Burk et al, 1988; Haggar & Froelich, 1988).

Therefore, a complete staging of a bone tumour requires both short TR/TE and long TR/TE SE sequences, as previously recommended (Richardson et al, 1986; Sundaram et al, 1986; Zimmer et al, 1986; Boyko et al, 1987; Cohen et al, 1988).

Primary bone tumours have been evaluated by many investigators using SE sequences (Cohen et al, 1984, 1988; Zimmer et al, 1985, 1986; Daffner et al, 1986; Richardson et al, 1986; Sundaram et al, 1986; Berquist, 1987; Boyko et al, 1987; Pettersson et al, 1987, 1988; Gillespy et al, 1988; Kanal et al, 1988) but only a few reports are available about the use of the STIR sequence in this clinical situation (Porter et al, 1987; Colman et al, 1988).

The STIR sequence, with its fat signal suppression, has been previously evaluated in liver disease (Bydder et

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al, 1985) and in orbital lesions (Atlas et al, 1988). Its employment is likely to be useful in studying tissues with a high content of adipose tissue such as yellow bone marrow. The STIR sequence also produces a high signal response from tissues with long T_1 and T_2 relaxation times, increasing its sensitivity in tumour detection (Bydder & Young, 1985; Porter et al, 1987; Young, 1987).

Table I. Histologic groups of lesions studied ($n = 60$)

Tumours of osteoblastic differentiation ($n = 26$). Mean age: 19.4 years (range 8–56)	
Aggressive osteoblastoma: Scapula	1
Osteosarcoma:	21
Femur	10[a]
Tibia	7[a]
Humerus	2[a]
Fibula	1
Ischium	1[b]
Parosteal osteosarcoma:	3
Femur	2
Tibia	1[a] (R)
Periosteal osteosarcoma Tibia	1
Tumours of chondroid differentiation ($n = 10$). Mean age: 42 years (range 18–58)	
Osteochondroma:	3
Scapula	1 (R)
Humerus	1 (R)
Femur	1 (R)
Chondrosarcoma:	6
Femur	3 (R)
Tibia	2 (R)
Paranasal sinus	1 (R)
Benign chondroblastoma:	1
Humerus	1
Fibrous tumours ($n = 5$). Mean age 35 years (range 16–53)	
Desmoplastic fibroma: tibia	1
Malignant fibrous histiocytoma	4
Femur	2
Ilium	1
Toe-phalanx	1
Giant cell tumours ($n = 4$). Mean age: 42.5 years (range 25–84)	
Femur	4
Ewing's sarcoma ($n = 13$). Mean age: 16.6 years (range 3–27)	
Femur	8[a] (R)
Tibia	1
Ulna	1[a]
Sacrum	1[a]
Ilium	2
Tumours arising in tissue rests ($n = 3$). Mean age: 44 years (range 25–65)	
Chordoma	2 (R)
Ameloblastoma	1

[a] Studies performed twice, in pre- and post-chemotherapy phase ($n = 8$).
[b] Tumour arising in bone affected by Paget's disease ($n = 1$).
(R) Studies performed for detecting recurrences ($n = 9$).

The MRI findings in 60 patients with primary bone tumours were all studied to compare the usefulness of STIR and SE sequences. The accuracy of both MRI techniques in defining tumour extent has been compared with pathology macroslides in 24 patients.

Patients and method

A total of 68 MRI studies for primary bone tumours performed in 60 patients between January 1987 and April 1989 were reviewed (Table I). All patients underwent one MRI examination and eight patients underwent two examinations, the later scan performed after pre-operative chemotherapy to assess the tumour response. Among the patients studied only once, nine were studied after surgery for suspected recurrence.

In 24 patients who underwent MRI examinations immediately (within 10 days) before surgery, a comparison between MRI images and macroslides of surgical specimens was performed, particularly for intramedullary tumour extent (Table II).

All MRI examinations were performed with a Picker International 0.5 T Superconducting Body Scanner operating at 21.3 MHz. In all patients, MRI spin-echo studies were performed using short TR/TE of 700–800/26/2–4 (TR/TE/number of repetitions) and long TR/TE of 2000/80/2. The STIR sequences were performed using TR of 1800–2200 ms and inversion times (TI) of 120–130 ms. The TI value was selected for the purpose of nulling the signal of fat, based on its T_1, as previously reported (Bradley et al, 1983; Bydder & Young, 1985; Bydder et al, 1985; Porter et al, 1987; Young, 1987).

All diagnoses were confirmed by needle biopsy or surgical excision, or by follow-up after 1 year. In the cases in which a comparison with pathologic macroslides was performed, the measurements of intramedullary tumour extent were obtained (Gillespy et al, 1988) by tracing the neoplastic contours on the macroslide films with a fine tipped pen and then measuring the major longitudinal tumour axis. On MRI images the measurement of intraosseous tumour extent was easily

Table II. Results of MRI compared with post-surgical macroslides ($n = 24$) (*i.e.* MRI studies immediately before surgery)

Studied only after chemotherapy (four cases)	
Ewing's sarcoma	3
Osteosarcoma	1
Studied before and after chemotherapy (six cases)	
Osteosarcoma	3
Ewing's sarcoma	3
Studied before surgery, without previous chemotherapy (14 cases)	
Giant cell tumours	3
Osteochondroma	2
Chondrosarcoma	6
Desmoplastic fibroma	1
Parosteal osteosarcoma	2

obtained using the centimetre scale recorded on each film as a reference point.

Results

Presence of tumour

In all cases the STIR sequence provided a clear demonstration of the tumours, which appeared markedly hyperintense, regardless of their benign or malignant nature. No false negative results were observed with the STIR sequence (*i.e.* sensitivity 100%) by comparison with SE scans which failed to identify two small recurrent lesions, a chondrosarcoma in the femoral head and an osteochondroma of the coracoid process of the scapula.

In cases after surgery, in whom the anatomical landmarks were altered, both STIR and SE sequences demonstrated all lesions, but these were much more conspicuous on the STIR sequence. Furthermore, in one case of osteosarcoma secondary to Paget's disease, the STIR sequence alone defined the exact extent of the neoplasm (Fig. 1) which appeared as a bright area well demarcated from the surrounding dysplastic bone. The SE sequences showed a mass effect, without defining the limits of the lesion against a background of multiple bone inhomogeneities.

Intramedullary extent

Fat signal was consistently suppressed on STIR images at T_1 of 120–130 ms in all studies, with yellow bone marrow appearing as a homogeneous low SI background. The SI was particularly low when yellow fatty marrow was present, and appeared less hypointense in relatively active hematopoiesis (red marrow) with its lower fat : cellular ratio (Kanal et al, 1988).

Because of the exclusive suppression of signal from marrow fat, and for the high SI of medullary tumours, the involvement of the medullary cavity was well shown with the STIR sequence. In seven MRI studies performed in children, in whom conversion of marrow was incomplete, a scattered pattern of increased medullary signal was found, usually well differentiated from tumour.

The accuracy of the STIR sequence in depicting intramedullary neoplastic extent, as shown by comparison with macroslides, was equal to SE sequences, in 19 cases, and superior in five cases (20.8%).

Magnetic resonance imaging measurements obtained with both STIR and SE sequences correlated well with macroslides in all but two cases of Ewing's sarcoma, in which both STIR and SE sequences underestimated histological tumour extent. In these cases, both MRI studies could not define exactly the limits of the neoplasm, which gradually shaded into the normal SI bone marrow. On histologic comparison, tumour infiltration was found many centimeters farther than MRI detected limits, a scattered pattern of cellular clusters having replaced bone marrow, without bony trabecular destruction.

The STIR sequence clearly showed satellite lesions (skip metastases) better than SE sequences in two cases.

Soft tissue invasion

Because of the exclusive nulling of the signal from fat, muscle SI appears on the STIR sequence to be slightly increased relative to normal bone marrow, but markedly lower compared with tumour, allowing a good differentiation between extraosseous and intraosseous tumour components.

In 37 of 54 cases of malignant bone tumours (68.5%) the STIR sequence demonstrated an ill-defined increased SI in surrounding muscles subsequently proved not to be infiltrated by the tumour (*i.e.* the tumour appeared histologically to be contained beneath the periosteum). The change on the STIR sequence was attributed to tissue oedema and could be differentiated from direct tumour invasion by the absence of mass effect and by a slightly reduced SI compared with the tumour. This feature was not seen on the STIR

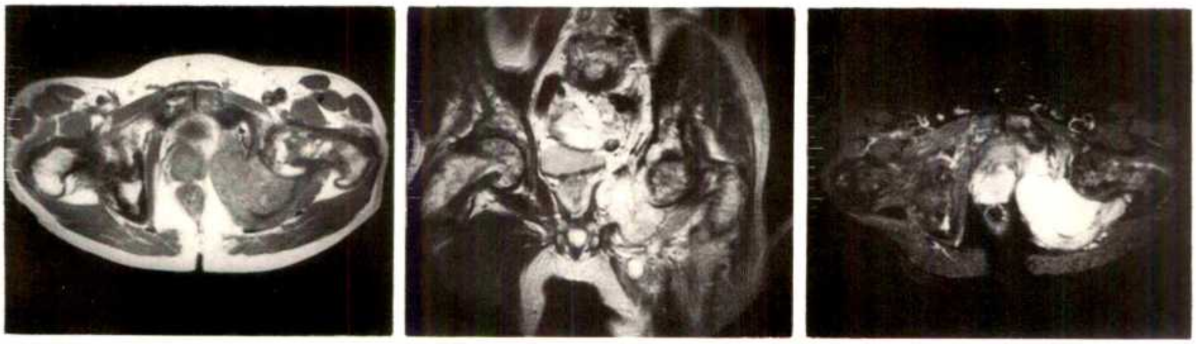
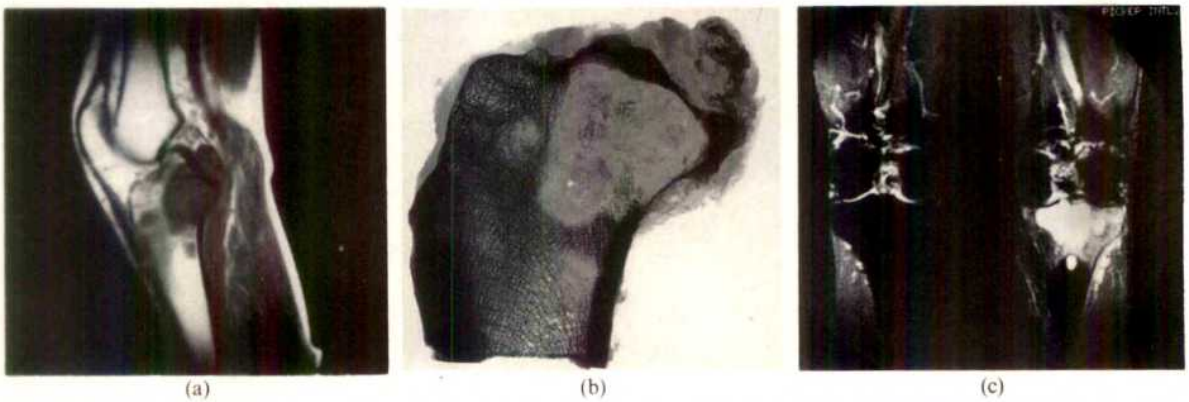

(a) (b) (c)

Figure 1. Left ischium osteosarcoma secondary to Paget's disease in a 76-year-old patient. (a) Axial 26/1100 SE sequence and (b) Coronal 80/2200 SE images. A large soft-tissue extent is present in the left ischiorectal fossa, with displacement of rectum and bladder. Multiple signal inhomogeneities in both femoral head, ilium and ischium as a result of Paget's disease are present, without clear evidence of intraosseous tumour component. (c) Axial STIR: demonstration of the intraosseous extent of the neoplasm, involving ischium and acetabulum.



(a) (b) (c)

Figure 2. Grade II chondrosarcoma of the left tibial plateau in a 58-year-old male. (a) Sagittal 22/700 SE sequence depicting the posterior multinodular lesion, which encases the posterior cruciate ligament; there is no clear evidence of cortical breakthrough or subperiosteal spread. (b) Surgical macroslide, sagittal plane. The tumour has diffusely replaced the bone marrow and involved the cortical bone; a large subperiosteal spread both in the tibial plateau and along the posterior surface of the metaphysis is also evident. This extraosseous spread was not well detected in (a). (c) Coronal 120/2000 STIR sequences better demonstrating both the diffuse permeation of marrow spaces in the lateral aspect of tibial metaphysis and the extraosseous tumour component, extending beneath the periosteum along the lateral surface.

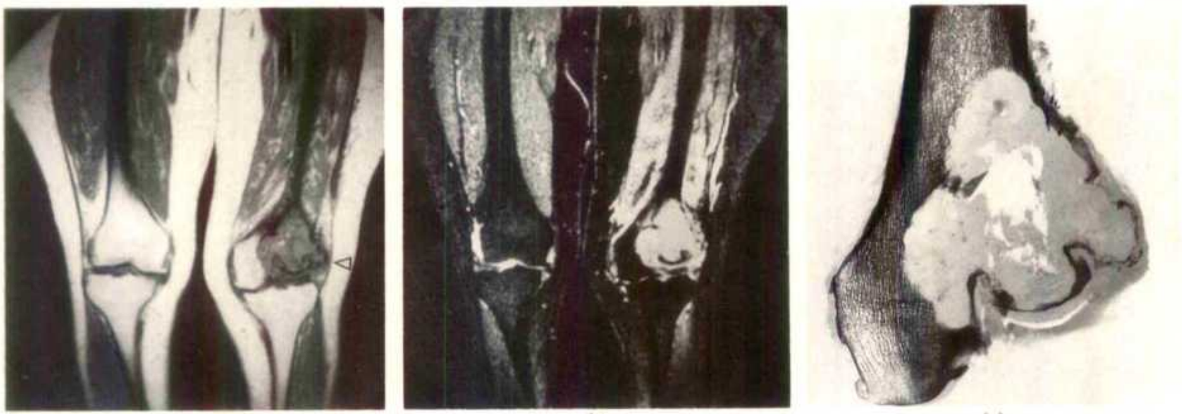
sequence around any of the benign tumours, even in one osteochondroma with a large soft-tissue extension. Peritumorous oedema was seen on long TR/TE sequences in seven cases (12.9%) of malignant bone marrows. The bright signal due to soft tissue oedema was easily differentiated from that due to bleeding caused by recent biopsy in 10 cases, which was usually more localized, mainly extending beneath the periosteum.

The STIR sequence highlighted joint effusion in 26 cases. In the same cases, SE sequences demonstrated the fluid collection in only 19 patients.

Discussion

The value of MRI in bone tumours resides mainly in its sensitivity to the presence of neoplastic tissue and in delineating its extent, both requirements satisfied by the STIR as well as by spin–echo sequences.

In the evaluation of bone tumours, the STIR sequence has specific advantages compared with conventional SE imaging, conferred on it by its higher sensitivity to tissue with prolonged T_1 and T_2 relaxation times and its ability to suppress soft-tissue fat signal intensity.



(a) (b) (c)

Figure 3. Giant cell tumour in the left lower femur of an 85-year-old male. (a) Coronal 26/1000 SE sequence: excellent morphological demonstration of the tumour extending to the articular surface and along the external contour of the lateral epicondyle (arrowhead). The cortical and subperiosteal spread is not clearly shown however. (b) Coronal 120/2200 STIR sequence: the outline of the tumour, and particularly the erosion of the lateral cortex, is better demonstrated than in (a). (c) Surgical macroslide, coronal plane.

In our series, the short TR/TE SE sequences provided the greatest spatial resolution and therefore a better depiction of anatomical details. Among the conventional SE sequences they are also the most reliable in showing intramedullary tumour extent. The combined use of both STIR and short TR/TE sequences provides greater accuracy in assessing intramedullary tumour extent, as confirmed by the comparison with surgical macroslides. The only exception in our series was represented by two cases of Ewing's sarcomas, whose intramedullary spread was underestimated by both sequences, mainly because of the peculiar infiltrative growth pattern of this type of tumour (Pringle, 1987).

The STIR sequence appeared to be more sensitive than short TR/TE SE scan to the spread of tumour beneath the periosteum, into adjacent soft tissues and in detecting joint effusions. Compared with short TR/TE SE scans, the STIR sequence usually provides characteristically "noisy" images owing to the low proton signal achieved after fat signal suppression, but its higher noise level is compensated by an extreme sensitivity in detecting lesions. In our series two small foci of recurrent tumour escaped detection by conventional SE sequences, but were identified by the STIR sequence, an important advantage when anatomical landmarks have been destroyed by surgery. Similarly, in one case of osteosarcoma arising from Paget's disease, only the STIR sequence was able to define the exact bony extent of the neoplasm. The STIR sequence is preferable to conventional long TR/TE sequences, which discriminate poorly between tumour and intramedullary or soft-tissue fat, in definition of neoplasm extent.

The higher sensitivity of the STIR sequence in highlighting tissue with a prolongation of T_1 and T_2 relaxation parameters makes this sequence less specific. Other pathological conditions with long T_1 and T_2 relaxation times such as inflammatory reactions, fluid collections or simple peritumoral oedema are shown by STIR as high SI intensity areas. The STIR sequence demonstrated soft-tissue oedema in 68.5% of the malignant tumours in our series as a bright area extending beyond the tumour mass, making it difficult to define tumour limits, representing a potential risk of overstaging. This problem seems not to be specific for the STIR sequence, being observed also in conventional long TR/TE studies of soft-tissue malignancies (Beltran et al, 1987). The distribution of the signal and the gross morphology of the muscles can usually differentiate between tumour invasion and peritumoral oedema. In addition, information derived from the short TR/TE sequence can be used for comparison.

The ability of the STIR sequences to detect peritumoral oedema may aid detection of small neoplastic foci of dimensions below the limits of detectability of the MRI system. For this reason the STIR sequence may be suggested as a screening method in detecting recurrences. In our series, no peritumoral oedema was found around any of the benign tumours, which may be helpful in differentiating benign from malignant neoplasms.

False negative results have been reported with SE studies (Reuther & Mutschler, 1988); conversely, no false negatives were found in our series, tumour always being demonstrated on the STIR sequence.

The results of this survey indicate that short TR/TE and STIR sequences should both be used in the evaluation of primary bone tumours prior to treatment and in the follow-up if local recurrence is suspected. The two sequences should be performed in the same longitudinal plane to allow direct comparison of images. A further short TR/TE sequence in the axial plane may be useful for anatomical detail. The long TR/TE sequence can be fruitfully substituted by the STIR sequence in MRI examination of bone tumours.

References

ATLAS, S. W., GROSSMAN, R. I., HACKNEY, D. B., GOLDBERG, H. I., BILANIUK, L. T. & ZIMMERMAN, R. A., 1988. STIR MR imaging of the orbit. *American Journal of Roentgenology, 151*, 1025–1030.

BELTRAN, J., NOTO, A. M., CHAKERES, D. W. & CHRISTOFORIDIS, A. J., 1987. Tumors of the osseous spine: staging with MR imaging versus CT. *Radiology, 162*, 565–569.

BELTRAN, J., SIMON, D. C., KATZ, W. & WEIS, L. D., 1987. Increased MR signal intensity in skeletal muscle adjacent to malignant tumors: pathologic correlation and clinical relevance. *Radiology, 162*, 251–255.

BERQUIST, T. H., 1987. Bone and soft tissue tumors. In *Magnetic Resonance of the Musculoskeletal System*. Ed. by T. H. Berquist, R. L. Ehman & M. L. Richardson (Raven Press, New York), pp. 85–108.

BOYKO, O. B., CORY, D. A., COHEN, M. D., PROVISOR, A., MIRKIN, D. & DEROSA, G. P., 1987. MR imaging of osteogenic and Ewing's sarcoma. *American Journal of Roentgenology, 148*, 317–322.

BRADLEY, W. G., NEWTON, T. H. & CROOKS, L., 1983. Physical principles of nuclear magnetic resonance. In *Advanced Imaging Techniques*. Ed. by T. H. Newton & D. G. Pott (Clavadel Press, California, USA), pp. 15–61.

BURK, D. L. JR, DALINKA, M. K., SCHIEBLER, M. L., COHEN, E. K. & KRESSEL, H. Y., 1988. Strategies for musculoskeletal magnetic resonance imaging. *Radiologic Clinics of North America, 26*, 653–672.

BYDDER, G. M. & YOUNG, I. R., 1985. MR imaging: clinical use of inversion recovery sequence. *Journal of Computer Assisted Tomography, 9*, 659–675.

BYDDER, G. M., STEINER, R. E., BLUMGART, L. H., KHENIA, S. & YOUNG, I. R., 1985. MR imaging of the liver using short TI inversion recovery sequences. *Journal of Computer Assisted Tomography, 9*, 1084–1089.

COHEN, M. D., KLATTE, E. C., BAEHNER, R., SMITH, J. A., MARTIN-SIMMERMAN, P., CARR, B. E., PROVISOR, A. J., WEETMAN, R. M., COATES, T., SIDDIQUI, A., WEISMAN, S. J., BERKOW, R., MCKENNA, S. & MCGUIRE, W. A., 1984. Magnetic resonance imaging of bone marrow disease in children. *Radiology, 151*, 715–718.

COHEN, E. K., KRESSEL, H. Y., FRANK, T. S., FALLON, M., BURK, D. L. JR, DALINKA, M. K. & SCHIEBLER, M. L., 1988. Hyaline cartilage-origin bone and soft tissue neoplasms: MR appearance and histologic correlation. *Radiology, 167*, 477–481.

COLMAN, L. K., PORTER, B. A., REDMOND, J. III, OLSON, D. O., STIMAC, G. K., DUNNING, D. M. & FRIEDL, K. E., 1988. Early diagnosis of spinal metastases by CT and MR studies. *Journal of Computer Assisted Tomography*, *12*, 423–426.

DAFFNER, R. H., LUPETIN, A. R., DASH, N., DEEB, Z. L., SEFCZEK, R. J. & SCHAPIRO, R. L., 1986. MRI in the detection of malignant infiltration of bone marrow. *American Journal of Roentgenology*, *146*, 353–358.

GILLESPY, T. III, MANFRINI, M., RUGGIERI, P., SPANIER, S. S., PETTERSSON, H., & SPRINGFIELD, D. S., 1988. Staging of intraosseous extent of osteosarcoma: correlation of preoperative CT and MR imaging with pathologic macroslides. *Radiology*, *167*, 765–767.

HAGGAR, A. M. & FROELICH, J. W., 1988. MR imaging strategies in primary and metastatic malignancy. *Radiologic Clinics of North America*, *26*, 689–696.

KANAL, E., BURK, D. L. JR, BRUNBERG, J. A., JOHNSON, N. D., WOOD, B. P. & FLOM, L., 1988. Pediatric musculoskeletal magnetic resonance imaging. *Radiologic Clinics of North America*, *26*, 211–239.

PETTERSSON, H., GILLESPY, T. III, HAMLIN, D. J., ENNEKING, W. F., SPRINGFIELD, D. S., ANDREW, E. R., SPANIER, S. & SLONE, R., 1987. Primary musculoskeletal tumors: examination with MR imaging compared with conventional modalities. *Radiology*, *164*, 237–241.

PETTERSSON, H., SLONE, R. M., SPANIER, S., GILLESPY, T. III, FITZSIMMONS, J. R. & SCOTT, K. N., 1988. Musculoskeletal tumors: T_1 and T_2 relaxation times. *Radiology*, *167*, 783–785.

PORTER, B. A., OLSON, D. O. & STIMACK, G. K., 1987. STIR imaging of marrow malignancies. *SMRM Abstracts*, 146.

PRINGLE, J. A. S., 1987. Pathology of bone tumours. *Bailliere's Clinical Oncology*, *1*, 21–63.

REUTHER, G. & MUTSCHLER, W., 1988. Recurrence detection of malignant mesenchymal neoplasms in MRI versus CT. *ECR Abstracts*, 110.

RICHARDSON, M. L., KILCOYNE, R. F., GILLESPY, T. III, HELMS, C. A. & GENANT, H. K., 1986. Magnetic resonance imaging of musculoskeletal neoplasms. *Radiologic Clinics of North America*, *24*, 259–267.

SARTORIS, D. J. & RESNICK, D., 1987. MR imaging of the musculoskeletal system: current and future status. *American Journal of Roentgenology*, *149*, 457–467.

SUNDARAM, M., MCGUIRE, M. H., HERBOLD, D. R., WOLVERSON, M. K. & HEIBERG, E., 1986. Magnetic resonance imaging in planning limb-salvage surgery for primary malignant tumors of bone. *The Journal of Bone and Joint Surgery*, *68*, 809–819.

YOUNG, I. R., 1987. Advanced imaging techniques. In *Practical NMR Imaging*. Ed. by M. A. Foster & J. M. S. Hutchinson (IRL Press, Oxford), pp. 199–248.

ZIMMER, W. D., BERQUIST, T. H., MCLEOD, R. A., SIM, F. H., PRITCHARD, D. J., SHIVES, T. C., WOLD, L. E. & MAY, G. R., 1985. Bone tumors: magnetic resonance imaging versus computed tomography. *Radiology*, *155*, 709–718.

——1986. Magnetic resonance imaging of osteosarcomas. Comparison with computed tomography. *Clinical Orthopaedics and Related Research*, *208*, 289–299.

1990, *The British Journal of Radiology*, *63*, 257–262

The computed tomographic appearances and clinical significance of intussusception in adults with malignant neoplasms

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Abstract. The computed tomography (CT) appearances of intussusception in 14 patients and the clinical follow-up of this condition in 17 adults with known primary malignant neoplasms were retrospectively reviewed. The ages of the 11 men and six women ranged from 25 to 83 years. Nine patients had been treated for malignant melanoma and the others for various primary neoplasms. Intussusception on CT was characterized by thickening of the affected bowel segment in all 14 patients and by the presence of intraluminal fat density material in 13, a concentric ring or "target" lesion in four, and an intra-luminal soft-tissue mass in nine. Five patients had intussusception, without other evidence of disease, caused by metastases in three patients, lipoma in one and idiopathic in one. Eleven of the other 12 patients had extensive disease, and one had small bowel cytomegalovirus infection. Five of these patients had more than one site of bowel involvement. Ten of the 12 patients had progression of disease on follow-up CT examinations and six died between 26 days and 7 months after diagnosis of intussusception. Intussusception may occur as the first indication of tumour recurrence or metastasis, but is more commonly a manifestation of widespread disease. However, even in patients with malignant neoplasms, it may be idiopathic or a result of benign neoplasm.

Adult intussusception occurs rarely, accounting for 5–16% of all cases of intussusception in North America (Agha, 1986; Felix et al, 1976). Unlike the childhood condition, more than 80% of adult cases are caused by a demonstrable bowel abnormality, and approximately 40% by a primary or secondary malignant neoplasm (Weilbaecher et al, 1971; Nagorney et al, 1981). The radiologic findings of intussusception on barium studies are well known. However, CT is now widely used in the evaluation of abdominal masses and nonspecific abdominal pain and may be the first examination performed in a patient in whom an intussusception is present. The computed tomographic (CT) findings have recently been described in a small number of short reports and in one series of nine patients (Merine et al, 1987). The CT findings are sufficiently characteristic to warrant a confident diagnosis based on this radiologic appearance alone. In this report, we have reviewed the case histories of 17 patients with known malignancy in whom a radiologic diagnosis of intussusception was made by CT, barium studies or both in order to re-emphasize the CT pattern and to evaluate the clinical significance of this radiologic diagnosis in patients from a centre treating cancer.

Materials and methods

The clinical records and radiologic examinations of 17 patients diagnosed as having intussusception of the small intestine or colon were retrospectively reviewed. The diagnosis had been made by CT in 14 patients, by barium studies alone in three and by both in 10. In 10 patients, CT was the initial or only method of examination. The intussuscepted bowel segment was resected in eight patients.

There were 11 men and six women, aged 25–83 years (mean 50.7 years). All patients had a known malignant neoplasm: nine had malignant melanoma, two had lymphoma, and one each had ovarian, colon, and duodenal cancer. Two patients had been treated for two primary neoplasms: one woman had been treated for both breast and ovarian primary tumours, and a man had both malignant melanoma and a bladder tumour. The remaining patient had acquired immune deficiency syndrome (AIDS)-related Kaposi's sarcoma of the chest wall.

The CT examinations were evaluated to characterize the appearance of the intussusception. Patient records and other imaging studies were reviewed to determine the extent of disease at the time of intussusception and to assess the course of each patient's disease.

Results

The intussuscepted segment was located in the small bowel in 13 patients, in the colon in two, in the ileocecal region in one and at the site of an ileocolic anastomosis in the remaining patient.

On CT intussusception was characterized by thickening of the affected bowel segment in all 14 patients examined (Figs 1–5). Thirteen patients had fat density material within the abnormal loop of bowel (Figs 1–4), located eccentrically in 12 cases and centrally in one. There was a concentric ring or "target" appearance in four lesions (Fig. 1), and nine patients had an almost homogeneous intraluminal soft-tissue mass at one end

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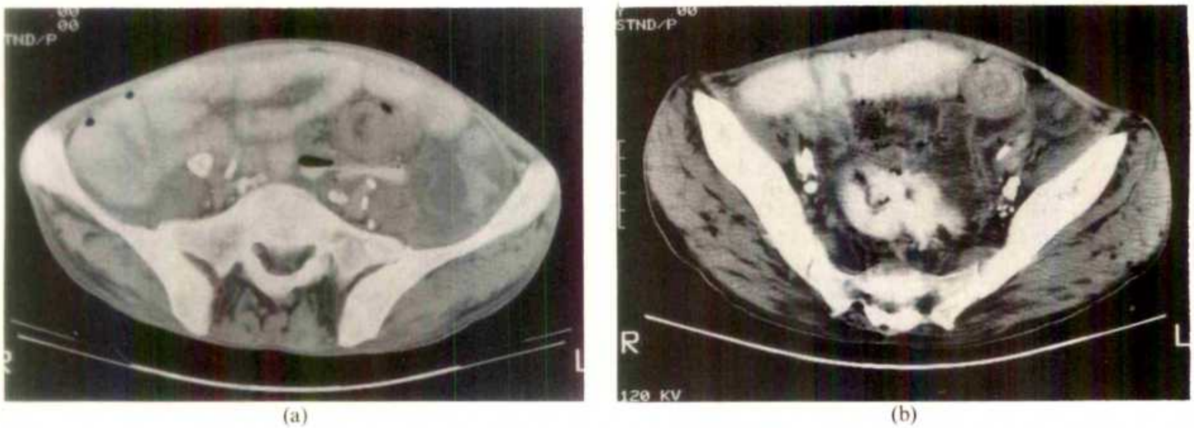
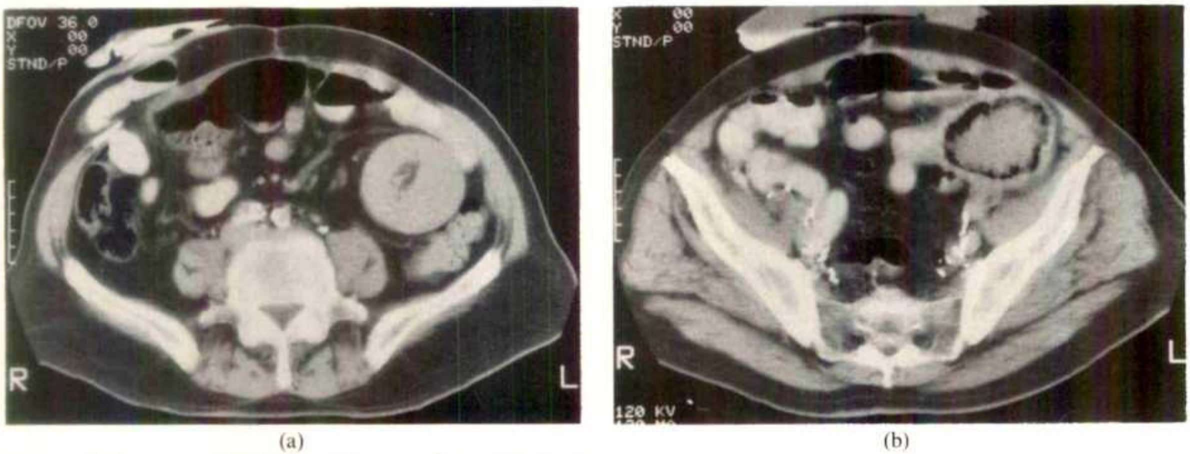


Figure 1. A 25-year-old asymptomatic man with Hodgkin's lymphoma. (a) Pelvic CT scan showing thickening of small bowel with an intraluminal soft-tissue mass and a small eccentric focus of fat density, and (b) CT scan 2 cm distally showing "target" lesion in small bowel with proximal small bowel dilatation and no contrast in the small bowel distal to the intussusception.

of the intussuscepted segment (Fig. 2). In one patient, the intussuscepting lesion was a colonic lipoma (Fig. 3). The length of the intussuscepted segment ranged from 1.6 cm to 9.0 cm (mean 5.9 cm). The intussuscepted bowel segment was oriented in the cranio-caudad direction in 10 patients (Figs 1 and 2), in the axial plane in two (Fig. 4) and had both cranio-caudad and axial components in the two remaining patients (Fig. 5).

Intussusception was the only radiologic abnormality in five patients. Surgery was performed on four of them



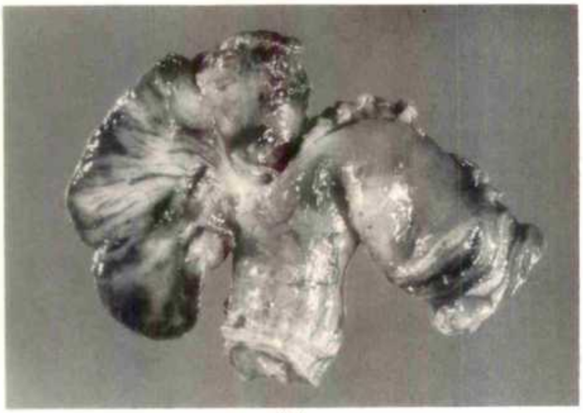


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Figure 2. An 83-year-old man with anaemia and constipation and a previous history of melanoma and sarcomatoid bladder carcinoma. (a) Abdominal CT scan showing thickening of a segment of small bowel with an eccentric focus of fat, and (b) 7 cm distal to (a), the lead point of the intussusception is surrounded by air. At operation an 8 × 3 cm intussuscepting polypoid mass caused by metastatic bladder carcinoma was resected.

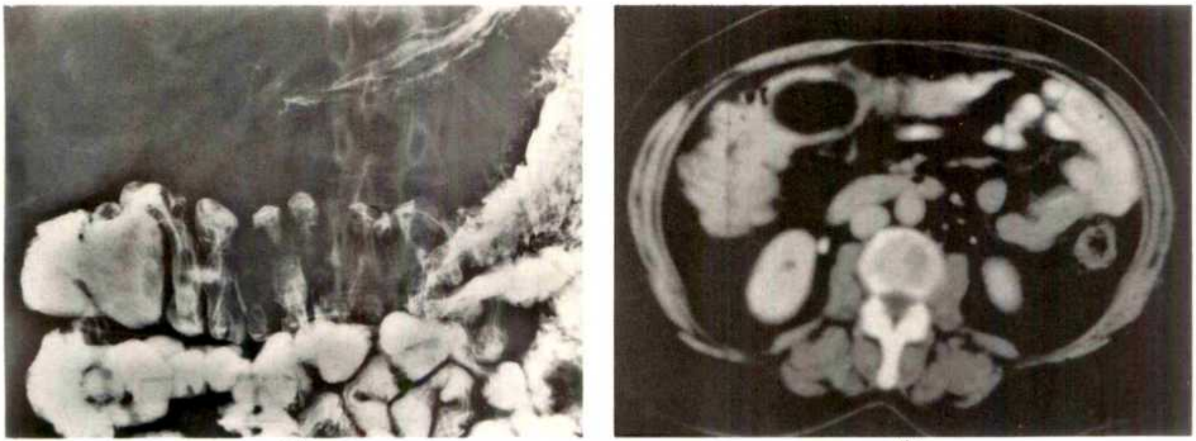
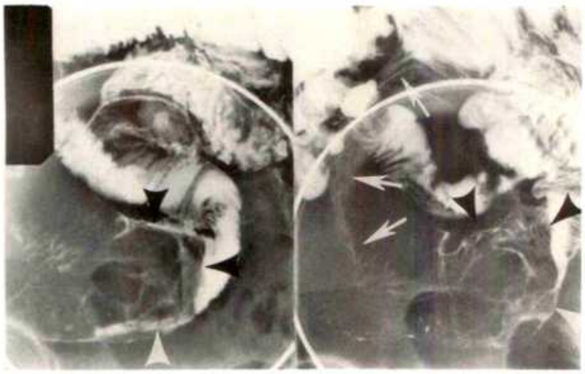

(a) (b)

Figure 3. A 53-year-old woman with abdominal pain, previously treated for breast and ovarian cancer. (a) Barium follow-through examination shows a smooth intraluminal mass in the transverse colon, and (b) CT scan through the mid-abdomen shows a well circumscribed intraluminal lipoma.

and confirmed the presence of intussuscepting small bowel metastases in three cases. These were caused by malignant melanoma in two patients and metastatic sarcomatoid bladder carcinoma in the third, who had been treated for both the bladder tumour and malignant melanoma (Fig. 2). In the fourth patient, who had previously been treated for breast and ovarian carcinoma, the pre-operative CT diagnosis of intussuscepting lipoma of the colon was confirmed (Fig. 3). These four patients had pain, gastrointestinal symptoms or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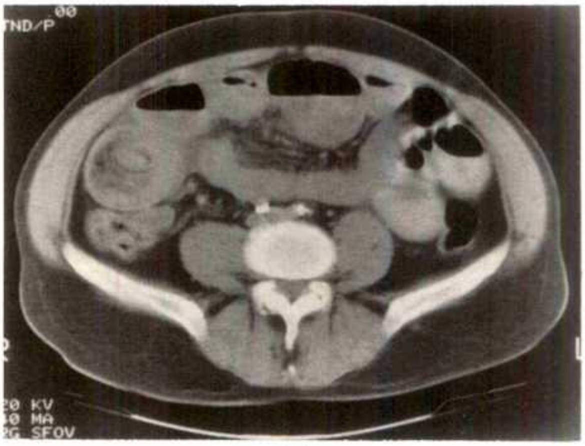

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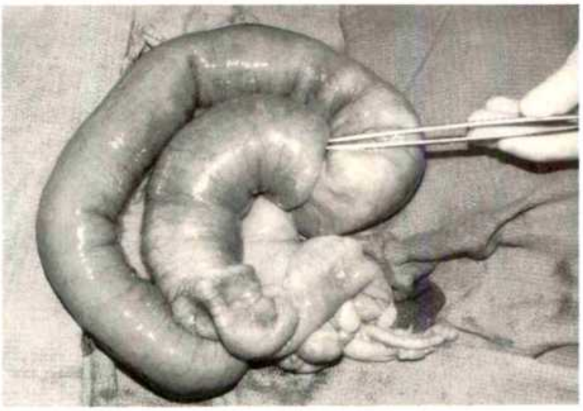
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Figure 4. A 60-year-old man with crampy abdominal pain and a past history of melanoma. (a) Barium follow-through examination showing small bowel dilatation with abrupt tapering of the lumen (arrows) as the intussusceptum invaginates into the distal bowel, ending in an intraluminal mass (arrowheads) within the more distal small bowel or intussuscipiens, and (b) CT scan through the proximal pelvis showing an intraluminal soft-tissue mass and fat in a dilated and thickened small bowel loop. At laparotomy, there was intussusception with proximal small bowel dilatation.

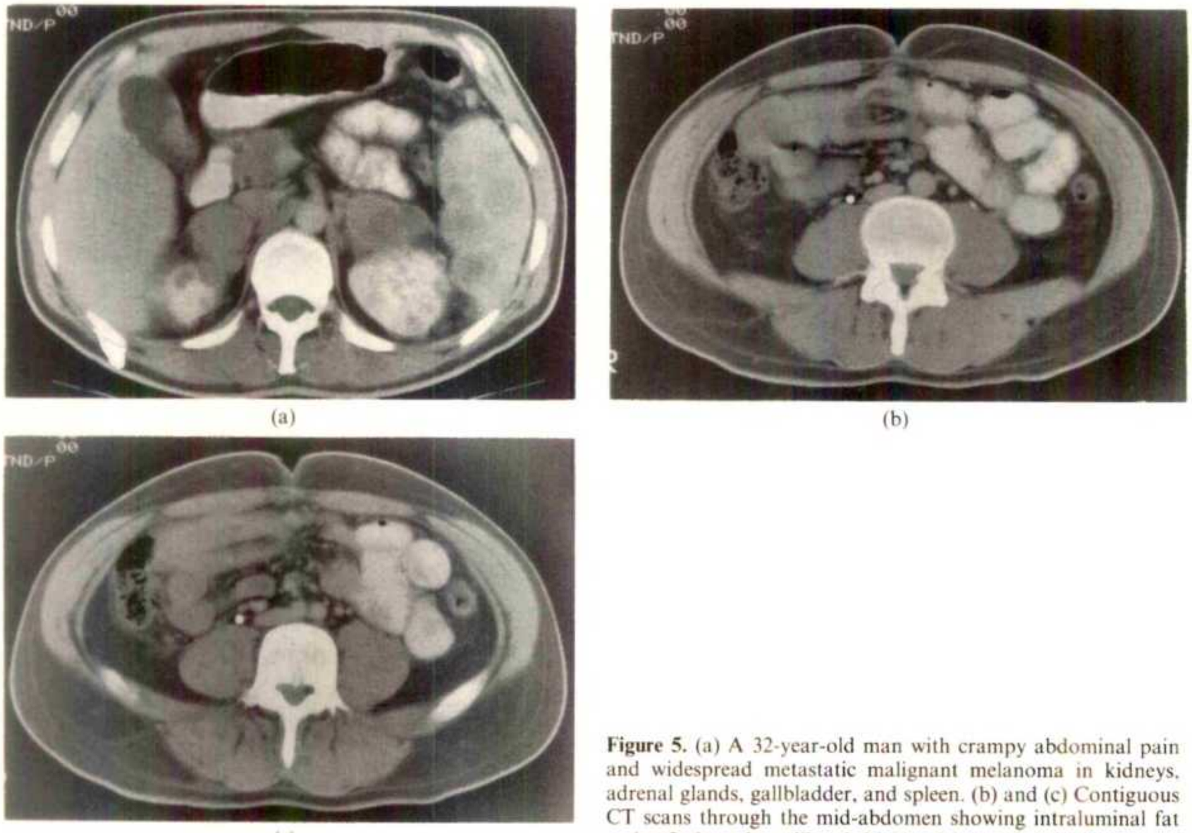
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Figure 5. (a) A 32-year-old man with crampy abdominal pain and widespread metastatic malignant melanoma in kidneys, adrenal glands, gallbladder, and spleen. (b) and (c) Contiguous CT scans through the mid-abdomen showing intraluminal fat and soft tissue in a dilated thickened loop of small bowel.

evidence of blood loss, and two had CT evidence of proximal small bowel dilatation at the time of intussusception. Three of these four patients have remained disease-free for 3–61 months after surgery. The other patient developed axillary nodal metastases 3 months after surgery but, following chemotherapy, had no measurable disease 8 months later. The fifth patient, who had previously had an ovarian neoplasm resected, was asymptomatic with no other evidence of disease at the time of CT and has remained symptom-free for a year.

In the other 12 patients, the intussuscepting lesion was one of many sites of disease at the time of diagnosis (Fig. 5). The intussusception was shown by CT in nine cases and by barium studies alone in three. In two of these three patients, the relevant area had not been studied by CT; in the other patient, CT examination had been normal 3 days earlier. Eleven of these patients had abdominal pain, non-specific gastrointestinal symptoms, or evidence of blood loss, and five had CT evidence of proximal small bowel dilatation. Eleven of them had radiologic evidence of extensive disease, including eight patients with extra-abdominal disease. Five patients had more than one site of bowel involvement. One patient, who had AIDS-related Kaposi's sarcoma of the chest wall, had cytomegalovirus involvement of the small bowel.

The intussuscepted segment of bowel was resected in four of these 12 patients; three of them had gastrointestinal bleeding and one had small bowel obstruction. One patient died 4 months after resection of a metastatic jejunal lesion from duodenal carcinoma. Of two patients with metastatic melanoma, one died 4 months after surgery and the second is alive with progression of pulmonary metastases 2 years after surgery. The fourth patient had stable abdominal lymphoma 5 months after surgery.

Ten of these patients had progression of disease on follow-up CT examinations and six of them died between 26 days and 7 months after diagnosis. Follow-up CT examination of the intussusception was available in four patients, two of whom had spontaneous resolution of the intussusception with no recurrence on subsequent examinations.

Discussion

The CT appearances of intussusception are characteristic and have been documented clinically and confirmed experimentally in animal models (Curcio et al, 1982; Donovan & Goldman, 1982; Iko et al, 1984; Merine et al, 1987). The major CT features are: (a) a thickened segment of bowel owing to invagination of one segment (the intussusceptum) into an adjacent enveloping segment (the intussuscipiens); (b) an eccentrically located low-density lesion owing to the fat content of the invaginated mesentery; (c) demonstration of the leading mass of the intussusceptum by air or barium (Curcio et al, 1982; Donavon & Goldman, 1982). We did not encounter the reniform lesions considered by Merine et al (1987) to be associated with focal bowel wall ischaemia, but none of the patients in our series had ischaemic lesions at laparotomy.

Intussusception in adults is rare in Britain and North America, but the prevalence and the causes of this condition show considerable regional variation throughout the world (Bond & Roberts, 1964; Elebute & Adesola, 1964; Murdoch & Wallace, 1977; Hadley & Simpson, 1983; The et al, 1987). For example, in the series of Nigerian patients described by Elebute and Adesola (1964) 42% were adults, and 92.5% of the intussusceptions were idiopathic. It has been suggested that this regional variation may be associated with enteric infections that are prevalent in certain tropical areas (Elebute & Adesola, 1964; Hadley & Simpson, 1983). One of the patients in our series had AIDS-related Kaposi's sarcoma of the chest wall and had profuse watery diarrhoea at the time of examination. A small bowel barium study showed intussusception, but a CT examination 3 days earlier was normal. At autopsy soon afterwards, no focal small bowel lesion was found, but there was diffuse involvement of the intestinal tract by cytomegalovirus. A similar case of intussusception has been reported by Balthazar et al (1986). Although small bowel intussusception due to local involvement by Kaposi's sarcoma may also occur (Khorshid et al, 1987), our case and the one reported by Balthazar et al were probably associated with enteric infection like the majority of cases in the tropics.

In addition to the patient with AIDS in whom there was documentation of transient intussusception, three other patients had definite radiologic findings of intussusception which either resolved on follow-up studies (two patients) or remained clinically silent with no radiologic follow-up (one patient). It is unclear if this represents idiopathic transient intussusception or is secondary to metastasis which has not progressed and which is no longer causing intussusception on follow-up studies. In the two patients with known stable metastasis, the latter is believed to be the case. In the patient who is free from known disease, the appearance is presumed to be idiopathic.

One other patient in this series, who had been treated for two primary neoplasms, had an intussusception which was unrelated to her known malignancy but resulted from benign colonic lipoma. This tumour is characterized by its negative attenuation on CT (Donovan & Goldman, 1982; McLaughlin et al, 1986; Hodgman et al, 1987) and more frequently occurs in women and on the right side of the colon (Castro & Stearns, 1972).

Three patients in our series had surgically proven intussusception as the only manifestation of metastatic disease. Eleven patients had documented widespread disease and the intussusception is assumed to represent a manifestation of metastasis. Four of these were confirmed surgically. Two resolved spontaneously as mentioned previously. The most common underlying malignancy was melanoma (nine patients) which is known to metastasize frequently to the gastrointestinal tract. In one autopsy series (Das Gupta & Brasfield, 1964) small bowel metastases were seen in 58% and colon metastases in 22% of patients. Metastases from melanoma to the small intestine are frequently polypoid (Das Gupta & Brasfield, 1964; Goldstein et al, 1977; Oddson et al, 1978) and thus are prone to intussusception, unlike, for example, metastases from primary lung tumours which more commonly present with perforation (McNeill et al, 1987). While melanoma is the most common metastasis to cause intussusception, it has also been reported as a manifestation of other neoplasms including leukaemia (Karakousis et al, 1974) renal cell carcinoma (Haynes et al, 1986), osteosarcoma (Webster & Arons, 1987), and squamous cell carcinoma of the lung (Listrom et al, 1988). We saw it in a case each of carcinoma of the colon, duodenum, bladder and ovary as well as in two patients with lymphoma. Lymphoma is a rare cause of intussusception in adults (Felix et al, 1976; Greco et al, 1986) but is more common in children over 6 years old (Wayne et al, 1976; Ein et al, 1986).

Surgical resection or decompression is the appropriate treatment for symptomatic adult intussusception (Weilbaecher et al, 1971; Nagorney et al, 1981). Surgical intervention may give useful palliation, even in patients with disseminated malignant disease, particularly if there is gastrointestinal bleeding or obstruction (Karakousis et al, 1974; Goodman & Karakousis, 1981; Klausner et al, 1982). Not surprisingly, those patients in our series whose disease was limited to solitary bowel metastases did very well after surgery and those with widely disseminated disease all progressed on follow-up studies with 50% mortality by 7 months after the noted intussusception. Two of four patients with widespread disease, however, derived useful palliation from surgical resection of the symptomatic intussuscepting metastasis.

In conclusion, intussusception is an uncommon complication of malignancy, but the possibility must be considered in the presence of even non-specific abdominal symptoms, particularly in a patient with melanoma, and the CT appearance must be recognized. The radiologic findings of intussusception may be the first indication of tumour recurrence or metastasis. However, even in patients with malignancy, some cases may be idiopathic, may resolve spontaneously or may be caused by a separate benign process. In the majority of instances, intussusception will be present in the context of widespread malignant disease and will be associated with a progressively downhill course.

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References

Agha, F. P., 1986. Intussusception in adults. *American Journal of Roentgenology*, *146*, 527–531.

Balthazar, E. J., Reich, C. B. & Pachter, H. L., 1986. The significance of small bowel intussusception in acquired immune deficiency syndrome. *American Journal of Gastroenterology, 81,* 1073–1075.

Bond, M. R. & Roberts, J. B. M., 1964. Intussusception in the adult. *British Journal of Surgery, 51,* 818–825.

Castro, E. B. & Stearns, M. W., 1972. Lipoma of the large intestine: a review of 45 cases. *Diseases of the Colon and Rectum, 15,* 441–444.

Curcio, C. M., Feinstein, R. S., Humphrey, R. L., Jones, B. & Siegelman, S. S., 1982. Computed tomography of enteroenteric intussusception. *Journal of Computer Assisted Tomography, 6,* 969–974.

Das Gupta, T. & Brasfield, R., 1964. Metastatic melanoma: a clinicopathological study. *Cancer, 17,* 1323–1339.

Donovan, A. T. & Goldman, S. M., 1982. Computed tomography of ileocecal intussusception; mechanism and appearance. *Journal of Computer Assisted Tomography, 6,* 630–632.

Ein, S. H., Stephens, C. A., Shandling, B. & Filler, R. M., 1986. Intussusception due to lymphoma. *Journal of Pediatric Surgery, 21,* 786–788.

Elebute, E. A. & Adesola, A. O., 1964. Intussusception in Western Nigeria. *British Journal of Surgery, 51,* 440–444.

Felix, E. L., Cohen, M. H., Bernstein, A. D. & Schwartz, J. H., 1976. Adult intussusception: case report of recurrent intussusception and review of the literature. *American Journal of Surgery, 131,* 758–761.

Goodman, P. L. & Karakousis, C. P., 1981. Symptomatic gastrointestinal metastases from malignant melanoma. *Cancer, 48,* 1058–1059.

Goldstein, H. M., Beydoun, M. T. & Dodd, G. D., 1977. Radiologic spectrum of melanoma metastatic to the gastrointestinal tract. *American Journal of Roentgenology, 129,* 605–612.

Greco, A., Leung, A. W. L., Zwi, L. J., Burdett-Smith, P., Spencer, J., Gibson, R. N. & Allison, D. J., 1986. Ileocolic intussusception in large cell lymphoma of the terminal ileum: report of a case. *Acta Radiologica: Diagnosis, (Stockholm), 27,* 687–690.

Hadley, G. P. & Simpson, R. L., 1983. Adult intussusception in the tropics. *British Journal of Surgery, 70,* 281.

Haynes, I. G., Wolverson, R. L. & O'Brien, J. M., 1986. Small bowel intussusception due to metastatic renal carcinoma. *British Journal of Urology, 58,* 460.

Hodgman, C. G., Lantz, E. J., Maus, T. P. & Conley, C. R., 1987. Computed tomography of intussusception due to colon lipoma. *Journal of Computer Assisted Tomography, 11,* 740–741.

Iko, B. O., Teal, J. S., Siram, S. M., Chinwuba, C. E., Roux, V. J. & Scott, V. F., 1984. Computed tomography of adult colonic intussusception: clinical and experimental studies. *American Journal of Roentgenology, 143,* 769–772.

Karakousis, C., Jolyoke, E. D. & Douglass, J. O., Jr, 1974. Intussusception as a complication of malignant neoplasm. *Archives of Surgery, 109,* 515–518.

Khorshid, K. A., Erzingatsian, K., Watters, D. A. K. & Bayley, A. C., 1987. Intussusception due to Kaposi's sarcoma. *Journal of the Royal College of Surgeons of Edinburgh, 32,* 339–340.

Klausner, J. M., Skornick, U., Lelcuk, S., Baratz, M. & Merhav, A., 1982. Acute complications of metastatic melanoma to the gastrointestinal tract. *British Journal of Surgery, 69,* 195–196.

Listrom, M. B., Davis, M., Lowry, S., Williams, W. W., Monsein, L. H., Kleinman, R. & Gogel, H. K., 1988. Intussusception secondary to squamous carcinoma of the lung. *Gastrointestinal Radiology, 13,* 224–226.

McLaughlin, S. J., Gray, J. G. & Braithwaite, M., 1986. Diagnosis of a right iliac fossa mass by computed tomography. *British Journal of Radiology, 59,* 623–624.

McNeill, P. M., Wagman, L. D. & Neifeld, J. P., 1987. Small bowel metastases from primary carcinoma of the lung. *Cancer, 59,* 1486–1489.

Merine, D., Fishman, E. K., Jones, B. & Siegelman, S. S., 1987. Enteroenteric intussusception: CT findings in nine patients. *American Journal of Roentgenology, 148,* 1129–1132.

Murdoch, R. W. G. & Wallace, J. R., 1977. Adult intussusception in Glasgow 1968 1968–74. *British Journal of Surgery, 64,* 679–680.

Nagorney, D. M., Sarr, M. G. & McIlrath, D. C., 1981. Surgical management of intussusception in the adult. *Annals of Surgery, 193,* 230–236.

Oddson, T. A., Rice, R. P., Seigler, H. F., Thompson, W. M., Kelvin, F. M. & Clark, W. M., 1978. The spectrum of small bowel melanoma. *Gastrointestional Radiology, 3,* 419–423.

The, T. G., Naraynsingh, V. & Raju, G. C., 1987. Adult intussusception in Trinidad. *Journal of the Royal College of Surgeons of Edinburgh, 32,* 22–23.

Wayne, E. R., Campbell, J. B. & Kosloske, A. M., 1976. Intussusception in the older child—suspect lymphosarcoma. *Journal of Pediatric Surgery, 11,* 789–794.

Webster, V. J. & Arons, I., 1987. Intussusception secondary to osteogenic sarcoma metastasis. *British Journal of Clinical Practice, 41,* 628–629.

Weilbaecher, D., Bolin, J. A., Hearn, D. & Ogden, W., 1971. Intussusception in adults. *American Journal of Surgery, 121,* 531–535.

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Does scrotal ultrasound reduce the need for orchidectomy in the clinically malignant testis?

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Abstract. Many recent studies have confirmed the ability of ultrasound to elucidate scrotal pathology, but its place in the work-up of specific testicular problems is not yet fully defined. We investigated 15 cases where a firm clinical diagnosis of testicular malignancy was made. All cases progressed to orchidectomy. Scrotal ultrasound refuted the diagnosis of malignancy in seven cases with subsequent histological proof of benignity. However, the nature and extent of the benign disease was such that, on review, orchidectomy was considered to be the most appropriate method of treating the patient. We contend that in the case of firm clinical diagnosis of testicular malignancy, an ultrasound diagnosis of benignity will not alter management, and it is therefore not an essential part of the work-up in this group of patients.

Testicular tumours are being diagnosed with increasing frequency, at an annual rate of 2.5–3/100 000 (Wallace, 1985). The clinical assessment of a testicular mass can be difficult, and appropriate surgical caution results in an over diagnosis of malignancy (Fowler et al, 1987; Kromann-Andersen et al, 1988). The accepted management of a clinically suspected testicular tumour is inguinal exploration which results almost invariably in orchidectomy. However, several recent studies have shown scrotal ultrasound to be up to 99% accurate in distinguishing benign from malignant masses (Scott et al, 1986; Fowler et al, 1987; Howe et al, 1988; London et al, 1989).

This study was undertaken to determine whether pre-operative ultrasound scanning should influence clinical management by reducing the number of orchidectomies performed in this group of patients.

Method

During a 12 month period, a prospective study was carried out on all patients presenting with scrotal swelling or pain. Only those with a testicular mass thought to be potentially clinically malignant were included. All examinations were performed by one surgical consultant and one senior registrar. Scrotal ultrasound was performed in each case as a pre-operative investigation by either the senior registrar or the consultant radiologist. Patients were scanned with a 5 MHz curvilinear phased array (Picker LSC 7000) using a 500 ml saline bag as a stand-off. The scrotal contents were elevated, for easier examination, by means of a simple tissue-paper "sling", the ends of which were held by the patient. Longitudinal and transverse scans were obtained and recorded on film using a Matrix Imager. Following orchidectomy the histological result was compared with the clinical and ultrasound diagnoses.

Results

Of 460 patients that were examined, only 15 met the criteria for the study. The ultrasound findings were classified as benign, malignant or indeterminate. The correlation with clinical assessment and histology are recorded in Table I. Ultrasound resulted in the diagnosis of seven cases of malignancy and seven cases of benign disease. The one indeterminate diagnosis was made on

Table I. Scrotal pathology group by ultrasound diagnosis compared with clinical diagnosis and histological result

Patient	Clinical diagnosis	Ultrasound diagnosis	Histology
1	M	M: unspecified	M: seminoma
2	M	M: unspecified	M: teratoma
3	M	M: unspecified	M: teratoma
4	M	M: unspecified	M: teratoma
5	M	M: unspecified	M: seminoma
6	M	M: seminoma	M: teratoma
7	M	M: seminoma	M: seminoma
8	M	B: epididymitis	B: epididymitis
9	M	B: epididymitis	B: epididymitis
10	M	B: abscess	B: abscess
11	M	B: infarct	B: abscess
12	M	B: orchitis	B: infarct
13	M	B: abscess	B: infarct
14	M	B: loculated hydrocoele	B: loculated hydrocoele
15	M	Indeterminate	M: seminoma

M = malignant.
B = benign.

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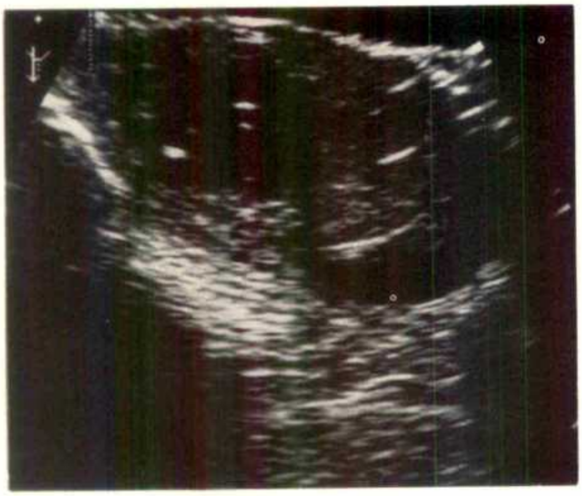

Figure 1. Longitudinal scan of testis showing the replacement of the upper pole by a partially cystic mass. Strong echoes within indicate calcification. The ultrasound diagnosis of an abscess was confirmed by histology. Note the reactive hydrocoele at the lower pole.

the basis of a homogenous reduction in echogenicity of a single testis which is known to represent either infection or infiltration (Rifkin, 1987). This was subsequently shown to be a seminoma. In the remaining 14 cases, where a definite ultrasound diagnosis was made, there was 100% correlation with histology in distinguishing benign from malignant disease, but ultrasound was not accurate in determining the nature of the benign disease. Tumour classification was only attempted in two cases and was correct in one.

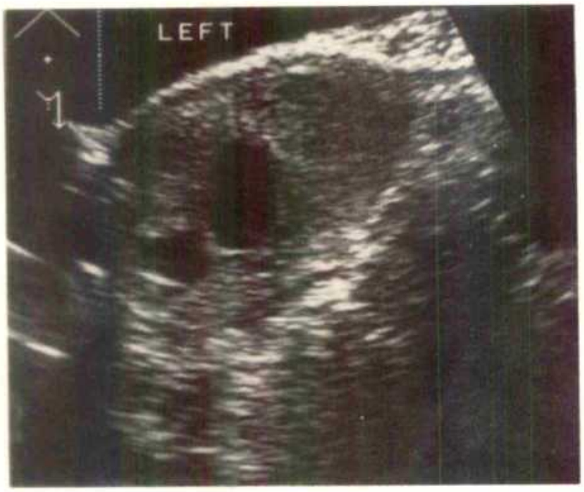

Figure 2. Longitudinal scan of testis showing the replacement of the upper pole by an expansile partially cystic mass. There is no evidence of internal calcification and no reactive hydrocoele. The ultrasound diagnosis was malignant; the histology suggested teratoma.

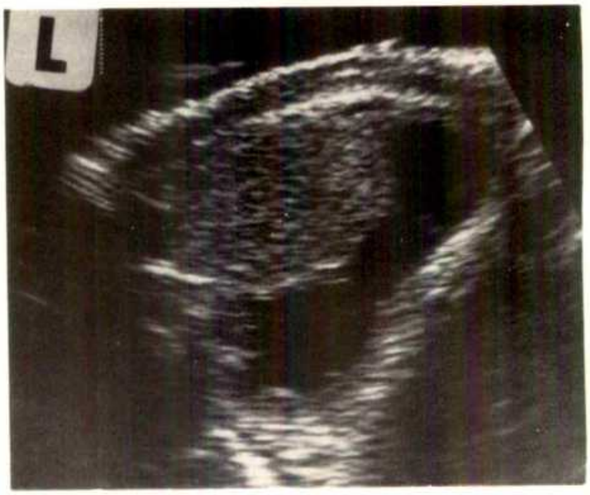

Figure 3. Longitudinal scan of testis showing loculated hydrocoele, confirmed by histology.

Discussion

This study supports the findings of other groups in demonstrating a consistent ability of ultrasound to distinguish benign from malignant testicular masses (Figs 1–4). In some cases the features could be worryingly similar, as Figs 1 and 2 show, but in others the ultrasound appearances were unequivocal, as demonstrated by Fig. 3. However, even in this case, sufficient clinical doubt remained at operation for orchidectomy to be performed.

The absolute need for an investigation can only be judged by whether it significantly influences clinical management, in this case surgical exploration of the scrotum. So far there has been no case where an ultra-

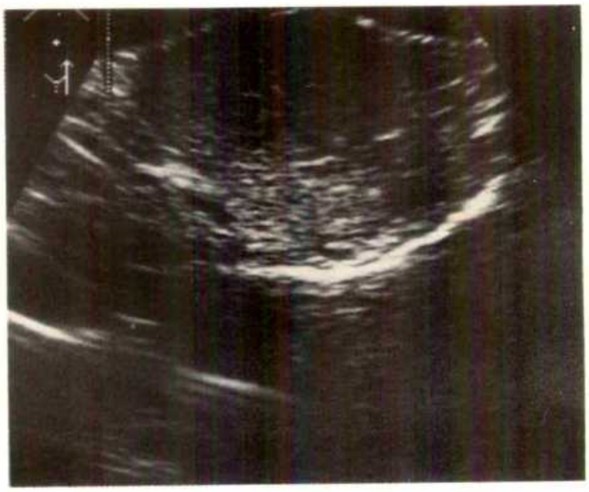

Figure 4. Longitudinal scan of testis showing expansile, poorly echogenic mass in mid-pole. The ultrasound diagnosis was seminoma, confirmed by histology.

sound diagnosis of benignity would have prevented orchidectomy, and it is pertinent to explore the possible reasons for this.

First, there is the entirely justifiable clinical concern of missing a potentially curable tumour, and there is a natural reluctance to rely on the results of a single investigation that contradicts the clinical diagnosis (this is especially true where life-threatening conditions are concerned).

Secondly, the removal of an infected or painful testicle offers a rapid cure for the patient in the absence of malignancy, and the mortality and morbidity of this procedure is low in otherwise fit patients (most in this group will be young).

Thirdly, it may be reassuring for the surgeon to be aware of the probable nature of the testicular mass, but it does not alter the surgical approach.

Fourthly, the impact of the diagnosis on the patient must be considered, and this is much more difficult to quantify. Confirmation of malignancy may reinforce the patients' trust in the clinical management. However, if the ultrasound diagnosis is benign supported by subsequent histology, the patient may well question the need for his orchidectomy. Therefore it could be argued that unless reliance is placed on the results of this investigation, performing it could be more of a hindrance than a help.

These negative points do not detract from the positive benefits of scrotal ultrasound, particularly in the case of a sole remaining testis or in the case of an equivocal diagnosis of malignancy, where a "wait and see" policy may be disastrous.

In conclusion, we have found that ultrasound does distinguish benign from malignant scrotal masses, but based on the points discussed above, we do not feel that its absence in the pre-operative work-up impedes effective management of the clinically malignant testicle.

Acknowledgments

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References

Fowler, R. C., Chennells, P. M. & Ewing, R., 1987. Scrotal ultrasonography: a clinical evaluation. *British Journal of Radiology, 60*, 649–654.

Howe, D., Foster, M. E., Gateley, C., Sturdy, D. E. & Griffiths, G. J., 1988. The clinical value of scrotal ultrasound in the investigation of scrotal pathology. *British Journal of Urology, 62*, 263–266.

Kromann-Andersen, B., Hansen, L. B., Larsen, K., Lawetz, K., Lynge, P., Lysen, D., Pors Nielson, S., Stockholm, K. H. & Foged, P., 1988. Clinical versus ultrasonographic evaluation of scrotal disorders. *British Journal of Urology, 61*, 350–353.

London, N. J. M., Kinder, R. B., Rees, Y. & Watkin, E., 1989. A prospective study of the value of routine scrotal ultrasonography in urological practice. *British Journal of Urology, 63*, 416–419.

Rifkin, M. D., 1987. Scrotal ultrasound. *Urologic Radiology, 9*, 119–126.

Scott, R. F., Bayliss, A. P., Calder, J. F. & Garvie, W. H. H., 1986. Indications for ultrasound in the evaluation of the pathological scrotum. *British Journal of Urology, 58*, 178–182.

Wallace, D. M. A., 1985. The testes and external genitalia. In *Essential Surgical Practice*, ed. by A. Cuschieri (Wright, Bristol), pp. 1200–1210.

1990, *The British Journal of Radiology*, *63*, 266–269

The range of bone density in normal British women

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Abstract. A study to determine the range of bone density in British females was carried out on a group of 165 normal women. The results showed an increase in mineral content with peak values occurring in the fourth decade (mean 1.06 g/cm^2; 95% confidence limits 0.783–1.343) and subsequent decline with increasing age. There was no significant effect from any risk factor but strict exclusion criteria were applied. The results from each age group were compared with those from the USA and showed a difference in the timing of peak bone density (third decade for the USA). Age-matched, clinically well-defined normal controls should be used for comparison with groups of patients in future studies.

One of the most rapidly developing fields in medicine today is the detection and treatment of osteoporosis. As interest in this subject has grown, advances have been made in the methods used to detect its presence (Zelch & Sullivan, 1989). Whilst a great deal of work remains to be done, it has been shown in a prospective study that a low bone mineral content is associated with an increase incidence of fractures (Wasnich et al, 1985). New techniques for the precise measurement of bone mineral content and bone density have therefore been welcomed.

Dual energy X-ray absorptiometry (DEXA) has the ideal properties of obtaining precise measurements in a short time with minimal radiation exposure. The first UK data for reproducibility were reported recently (Cullum et al, 1989) and although the equipment has been in the UK for one and a half years now, a locally derived range of normal values has not been available. Many workers have shown that bone mineral content varies with differing geographical and racial factors (Cohn et al, 1977; Seto et al, 1988). Previous work using quantitative computerized tomography and single-photon absorptiometry suggested that British women had lower values than their American counterparts (Compston et al, 1988). In view of these findings and the importance of DEXA for the future screening of osteoporosis, we developed a study to establish a range of bone density from normal British women.

Subjects and methods

A total of 165 females of all ages from 4 to 80 years had bone mineral density of the lumbar spine (L1–L4) measured using a DEXA system (Hologic 1000). Healthy volunteers were recruited, the majority being referred by general practitioners with an interest in osteoporosis. Some were normal controls referred by paediatric and adult endocrinologists conducting ongoing studies involving bone mineral measurements.

A detailed medical and social history was obtained from all participants in order to analyse risk factors. No blood chemistry was taken as all women were healthy and asymptomatic. Strict inclusion and exclusion criteria were as follows:

Inclusions

British or UK parentage, caucasian, living in the UK

Fully mobile with no previous atraumatic fractures

Exclusions

No current medication other than the oral contraceptive pill

No previous medication for more than 1 month

No calcium supplementation

Not pregnant or trying to conceive; not lactating

No hormone replacement therapy at any time

No history of prolonged bed rest (6 weeks)

Women who smoked more than 20 cigarettes per day

Alcohol intake of more than 2 units per day

In addition to the above criteria, any woman with a history of anorexia, amenorrhoea, premature ovarian failure or any other ailment likely to affect bone metabolism was excluded. None of the women were athletes although some did take part in regular exercise up to a maximum of three times per week. The aim of these multiple exclusions was to define exactly the population under study so that an accurate correlation with other clinical groups could be made in the future.

Of the original 165 women, 69 had taken the oral contraceptive pill at some time during their life and 28 gave a history of possible osteoporosis in the family. Thirty women smoked regularly and a further 18 women admitted drinking more than 1 unit of alcohol per day.

The distribution of the age groups was as follows:

Age (years)	4–19	20–29	30–39	40–49	50–59	60–69	70+
Number	9	25	25	39	50	16	1

Within each age group (20–69 years), the results obtained were normally distributed. A lumbar spine scan from L1 to L4 was obtained with the Hologic 1000 absorptiometer. The patient was scanned in a standard position (Stein et al, 1988) and the results analysed by experienced operators. A single scan took approximately 8 min and the radiation exposure from this was 0.003 mSv (one sixteenth of a modern chest radiograph). Spinal radiographs were not considered necessary to exclude the presence of crush fractures as these could easily be identified with the high resolution of the instrument.

All results were collated and assessed by standard statistical methods using Student's t test, linear regression and confidence limits where appropriate. The results were expressed as bone mineral density, measured in grams per square centimetre.

Results

The precision of the system (coefficient of variation) was 0.5% *in vitro* (standard bone phantom) and approximately 0.9% *in vivo* (10 subjects scanned 10 times over 2 weeks); interoperator variability in scanning and analysis was less than 0.5%. As many centres use only the results of L2–L4, a comparison between this region and L1–L4 was made. This showed that there is a linear relationship between the two with an r value of 0.995 ($p < 0.001$). The equation relating the two sets of details is

$$\text{L2–L4} = 1.03(\text{L1–L4}).$$

The bone density results were grouped into 10 year age cohorts and the resulting mean and standard errors are shown (Table I). The 95% confidence limits are taken as an arbitary guide to define normal and abnormal. As the measurement of bone density is most relevant in the years around the menopause, more women from the ages 40–59 were selected for study. The combined results of 10 and 5 year age groups is displayed in Fig. 1, showing the means and 95% confidence limits.

The correlation of bone density *versus* age gave an r value of -0.47, showing the overall decline of mineral content with increasing age. However, this represents two populations, that of the premenopausal woman whose mineral content is fairly static, and that of the postmenopausal woman who is losing bone rapidly. This has limited use therefore when studying populations of patients in a defined age group.

There were nine subjects under the age of 20 years and, as this was only a small sample with a rapidly changing mineral content, the results were expressed in the form of a linear regression. The resulting r value was 0.89 ($p < 0.001$), showing the direct correlation of increasing bone density with age in the young.

Table I. Bone density results

Age	Mean bone mineral density (g/cm^2)	Standard error of the mean
20–29	1.058	0.012
30–39	1.048	0.020
40–49	1.063	0.020
50–59	0.929	0.018
60–69	0.797	0.027

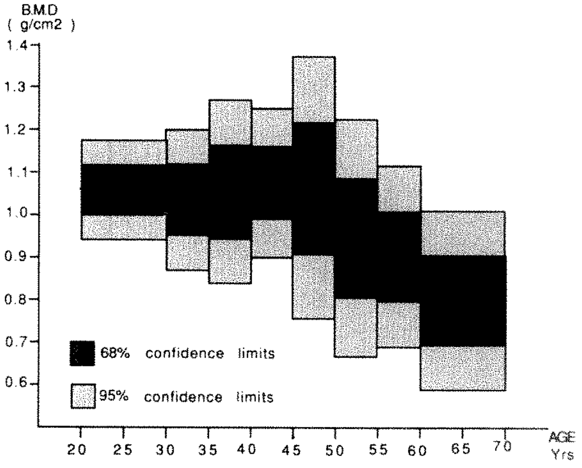

Figure 1. The range of bone density in normal British women.

Sixty-nine women were postmenopausal at the time of this study; as the age group 45–49 years included 16 premenopausal women and 12 postmenopausal women this group was studied further. The mean bone density of the premenopausal group was 1.114 g/cm^2, and the mean of the postmenopausal group was 0.99 g/cm^2. A two-tailed Student's t test gave a p value of 0.05, showing the major effect of the menopause on bone density.

An attempt to relate various factors to the final bone density in normal women showed few changes in our subjects. Those women who had taken the oral contraceptive pill were compared within each age group against those who had never taken it and also for women of similar menopausal status. There was found to be no significant difference at any age group and no difference between the users and non-users of either menopausal state.

The women who felt that there was a family history of osteoporosis were compared separately from all other women in the same age range and again there was no significant difference at any age. This may reflect the difficulty in obtaining an accurate assessment of the incidence of osteoporosis in the families studied and should be studied further with more accurate data from affected relatives.

There was no significant difference between these women with alcohol or tobacco consumption and those without. However, the numbers involved were small in both groups and the women most at risk were excluded from this study. The correlation of weight and bone density in premenopausal women was $r = 0.33$ ($p < 0.01$). The results for postmenopausal women show no significant correlation for height or weight with mineral density.

The British data were compared with those from the USA supplied with the instrument (Fig. 2), the bold lines representing the mean and 95% confidence limits for the US data. The US data are based on results from approximately 650 women and were collected from

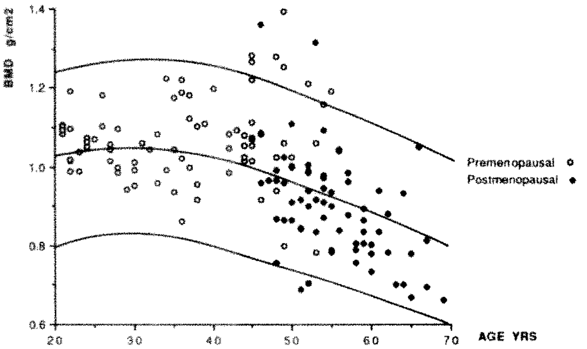

Figure 2. Comparison of US and UK data. The points are UK data and the curves represent US mean and two standard deviations.

several different centres. The mean and standard error of the mean from the UK and US data were compared in each age group. Whilst this showed no statistically significant difference for the two populations overall, the lower limits of statistical normality varied.

Discussion

The main advantages of DEXA over dual photon absorptiometry are the reduced scanning time and the improved precision (Stein et al, 1988). With DEXA there is no need for frequent source changes, the study is easy to analyse and it is readily understandable by those not used to the method. It is likely that DEXA will become the standard of the future in preference to single or dual photon absorptiometry.

Our results show that in British women bone mineral rapidly increases in relation to linear skeletal growth until the age of about 20 years. There is then a gradual increase with the highest values occurring early in the fourth decade in our study. Following the menopause, there is a progressive loss of bone mineral with increasing age.

Figure 2 shows that whilst British data are similar in many respects to the US population (Riggs et al, 1981) there are some differences. Our highest values occurred later, the mean bone density was greatest in the group 40–44 years and there was no discernable peak in the third decade, although longitudinal data are needed to confirm these initial findings.

For studies involving only British subjects, especially premenopausal women, we suggest using British control data for comparison. Where possible, if a restricted age group is to be studied, the data should be compared with those from women of similar age while possible risk factors should be well defined. The 95% confidence limits for each age group are more useful clinically and are preferable to the linear regression line produced for all ages.

Risk factor analysis showed no effect of smoking less than 20 cigarettes per day or drinking 2 units of alcohol per day. Those women with a family history of osteoporosis had normal bone densities, contrary to recent findings (Seeman et al, 1989), but validation of the truth of family histories was not possible. The use of the oral contraceptive pill produced no effect on the bone density at any age, unlike previous studies (Goldsmith & Johnson, 1975), although this may be a reflection of the changing dose of oestrogens being used.

It seems that the peak bone mass is largely determined by racial, genetic and geographical factors whilst the postmenopausal changes relating to the fall in oestrogen levels are more predictable whatever the population. Although the main use of bone mineral measurements is with menopausal women for the detection of osteoporosis, it should not be forgotten that there are other clinical groups whose management is influenced by mineral measurements. One such example is the young amenorrhoeic woman who may lose bone instead of gaining bone as expected for her age (Hall et al, 1989).

In conclusion, these are the first data on the range of bone density in normal British women as measured by DEXA. With increasing usage of DEXA, a national normal range with strict inclusion and exclusion criteria will be needed for future clinical use.

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References

Cohn, S. H., Abesamis, C., Yasumura, S., Aloia, J. F., Zanzi, I. & Ellis, K. J., 1977. Comparative skeletal mass and radial bone mineral content in black and white women. *Metabolism, 26* (2), 171–178.

Compston, J. E., Evans, W. D., Crawley, E. O. & Evans, C., 1988. Bone mineral content in normal UK subjects. *The British Journal of Radiology, 61*, 631–636.

Cullum, I. D., Ell, P. J. & Ryder, J. P., 1989. X-ray dual photon absorptionmetry: a new method for the measurement of bone density. *The British Journal of Radiology, 62*, 587–592.

Goldsmith, N. F. & Johnson, J. O., 1975. Bone mineral: effects of oral contraceptives, pregnancy and lactation. *The Journal of Bone and Joint Surgery, 57*, 657–668.

Hall, M. L., Davies, M. C., Jacobs, H. S. & Ell, P. J., 1989. Results from the first 212 patients studied using QDR bone densitometry. *Nuclear Medicine Communications, 10* (4), 217.

Riggs, B. L., Wahner, H. W., Dunn, W. L., Mazess, R. B., Offord, K. P. & Melton, L. J., 1981. Differential changes in bone mineral density of the appendicular and axial skeleton with aging. *Journal of Clinical Investigation, 67*, 328–335.

Seeman, E., Hopper, J. L., Bach, L. A., Cooper, M. E., Parkinson, E., McKay, J. & Jerums, G., 1989. Reduced bone mass in daughters of women with osteoporosis. *The New England Journal of Medicine, 320*, 554–558.

Seto, H., Nanbu, I., Banba, Y., Taki, K., Soya, T., Ihara, F., Kamei, T., Futatsuya, F. & Kakishita, M., 1988. Bone mineral density of the lumbar spine in Japanese: age related regression in normal subjects and a fracture threshold in osteoporotics. In *Proceedings of the Fourth Asia and Oceania Congress of Nuclear Medicine*, ed. by P. Shin-Hwa Yeh (Asia and Oceania Congress of Nuclear Medicine, Taiwan), p. 252.

Stein, J. A., Hochberg, A. M. & Lazewatsky, L., 1988.

Quantitative digital radiography for bone mineral analysis. In *Bone Mineral Measurements by Photon Absorptionmetry: Methodological Problems* (Leuven University Press, ISBN 90 6186 275 2), pp. 411–414.

WASNICH, R. D., ROSS, P. D., HEILBRUN, L. K. & VOGEL, J. M., 1985. Prediction of postmenopausal fracture risk with use of bone mineral measurements. *American Journal of Obstetrics and Gynaecology, 153* (7), 745–751.

ZELCH, J. V. & SULLIVAN, M. L., 1989. X-ray methods gain status in bone mineral analysis. *Diagnostic Imaging*, February, 106–110.

1990, *The British Journal of Radiology*, *63*, 270–277

Clinical study of relative biological effectiveness for cervical carcinoma treated by ^{252}Cf neutrons and assessed by histological tumour eradication

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Abstract. Clinical data of the University of Kentucky trial using californium (^{252}Cf), or caesium (^{137}Cs), are reviewed for dose–response based on the endpoint of tumour eradication estimated from hysterectomy specimens obtained 4–6 weeks after pre-operative irradiation. These data are used to assess the relative biological effectiveness (RBE) for ^{252}Cf neutrons compared with ^{137}Cs γ radiation. Tumours treated were of common stage but were of bulky or barrel shape suitable for "radiosurgical" therapy. Dose–response curves were constructed, and additional data from the literature used to analyse the curve shape. The photon dose–response curve is complex on a logarthmic plot, whereas the ^{252}Cf neutron curve is exponential. This indicates that the RBE can be different depending on the number of implants, schedule and size of dose delivered per session. The RBE values were approximately 8.0 at low doses or for multiple implants but they may rise to approximately 16 at larger doses or for single ^{252}Cf implants.

The reason for considering neutrons for brachytherapy (Maruyana, 1984; Maruyama et al, 1986) is based on the efficacy of neutrons to treat radioresistant tumours better than low linear energy transfer (LET) radiation such as X or γ rays (Gray et al, 1953; Fowler, 1986). For cervical cancers, radioresistance based on indirect evidence of hypoxia is well documented (Evans & Bergsjo, 1965; Bush et al, 1978; Watson et al, 1978). Californium is a neutron-emitting radionuclide suitable for clinical trials (Stoddard, 1986). Neutrons are effective against hypoxic cells and thus ^{252}Cf (Cf) should be of value for the therapy of tumours with established radioresistance (Hardt et al, 1982; Maruyama, 1984; Maruyama, 1988a). However, there is a problem in determining the appropriate neutron dose (Maruyama et al, 1985d) and a value for neutron RBE for tumours and normal tissues (Feola et al, 1982; Feola et al, 1986; Kal, 1986a, b). There is therefore a need to obtain better RBE data for determining what neutron doses can be prescribed for effective clinical tumour therapy.

The RBE of Cf neutrons for cervical cancer therapy in humans is still uncertain. Neutron and Cf studies have been performed with skin (Stone, 1948; Sheline et al, 1971; Yamashita et al, 1986), tumour regression (Vallejo et al, 1977; Maruyama, 1979; Maruyama & Muir, 1982; Maruyama et al, 1984; Parish et al, 1987), some other normal tissues (Cohen et al, 1985, 1989; Feola et al, 1986; Kal, 1986a, b) and with many cells and animals (Feola et al, 1982, 1986; Kal, 1986a); however, little direct RBE data exists for nearly all human tumours. In the fast neutron beam therapy studies conducted by the US Radiation Therapy Oncology Group (RTOG), no advantage was shown for neutrons and there was a very high complication rate in many normal tissues (Maor et al, 1988). Large volumes were irradiated. For Cf, the types and frequency of complications have been low and similar to that for photon therapy because of low integral dose. They occurred in only about 5% of treated patients (Maruyama et al, 1983, 1985b) and were exactly the same in type and frequency as for photon brachytherapy.

We have used estimated RBE values to guide our ongoing trials (Maruyama et al, 1983; Feola et al, 1986) but have sought more direct means to determine the RBE. In the present report, the RBE was estimated using the endpoint of tumour eradication from Stage IB bulky or barrel-shaped tumours treated by pre-operative radiation and extrafascial hysterectomy (Durrance et al, 1969; van Nagell et al, 1986), with residual tumour determined by careful histologic study of the hysterectomy specimen (Maruyama et al, 1982, 1985c, 1988b, 1989a). The aim of this study was to estimate a tumour RBE value for the biological effects of Cf for cervical cancer therapy. The merit of a working RBE value was to provide an approximate value to guide Cf treatments. We have used an RBE$_n$ value of 6.0 based on normal-tissue tolerance (Maruyama, 1984) without problems in our feasibility trials (Maruyama et al, 1988b). However, the working value for tumours has been studied further to determine a more accurate RBE value, and the preliminary results are presented in this paper.

Materials and methods

In this study we compare data for Stage IB bulky and barrel-shaped cervical cancer treated by caesium 137 (Cs) (Maruyama et al 1988b, 1989c) or Cf (Maruyama et al, 1989a) combined with fractionated whole-pelvis photon radiation therapy to 40–45 Gy with later hysterectomy as described by Durrance et al (1969). The surgical findings and the hysterectomy specimens were subsequently carefully examined for the presence or absence of residual, gross, or microscopic tumour (Maruyama et al, 1983). For this analysis, data from 53 Cf-treated cases (Maruyama et al, 1989a) and 80 Cs-treated patients (Maruyama et al, 1989c) are reviewed. The barrel-shaped tumour refers to a presentation of endocervical cancer with a widened cervical configuration originally described by Durrance et al (1969). Tumours were retrospectively reviewed. During 1976–1980 large tumours were first treated by Cf in a feasibility trial and its efficacy determined. We have reviewed our experience of all Cs and Cf patients treated between 1975–1987.

Patients were evaluated and treated at the University of Kentucky and their tumours staged by standard methods (Maruyama & van Nagell, 1982); the International Federation of Gynecology and Obstetrics (FIGO) system was used for staging (Kottmeier, 1979). Stage IB tumours were staged clinically and represent tumours confined to the cervix. Tumour diameter in centimeters was determined in all patients. Complete blood count, routine biochemical tests, chest radiograph, intravenous urogram and tumour biopsy were performed in all patients. The tumour was classified histologically as squamous cell carcinoma, adenocarcinoma (and variants) or small cell carcinoma. Blood transfusions were given if the following conditions existed: anemia; severe blood loss (transfusion as necessary); haemoglobin level less than 10 g/dl.

The radiotherapy methods have been reported (Coffey et al, 1986); linear accelerator X rays of 6–10 MV were delivered to the whole pelvis by ports approximately a minimum of 16 × 16 cm in size to a total dose of 40–45 Gy. The dose per fraction was 180 cGy a day; two to four fields were treated daily. Anterior–posterior, posterior–anterior, and right/left lateral fields were used. Additional boost radiation was given to the pelvic sidewalls to a minimum dose of 50 Gy using a centrally blocked portal.

For intracavitary therapy, sealed Cs or Cf sources were used; Cs emits 660 keV γ rays, Cf emits fast neutrons with a mean energy of 2.3 MeV and also high energy γ rays. Californium has a half-life of 2.65 years (Stoddard, 1986). The sources are encapsulated in iridium-platinum tubes 23 mm × 2.5 mm in size. The treatment with Cs was optimized and the dose of Cs was based on γ radiation (Maruyama et al, 1976; Maruyama & van Nagell, 1982); the dose of Cf was calculated taking into account the neutron dose (D_n) and γ ray dose (D_γ) (Maruyama, 1984). In these trials RBE or efficacy compared to an identical dose of γ radiation was assumed to be 6.0 for neutrons for normal tissues. Therapy with Cs sources was delivered in 48–72 h; therapy with Cf was delivered in 8–10 h. Standard afterloading applicators (Fletcher) were used for Cs and 60–75 mg equivalents of Cs was used; 125–200 μg of Cf was used in modified Henschke and locally designed applicators for Cf. Controlled access brachytherapy facilities, afterloading methods and use of special handling methods allowed Cf to be used for treatments without undue problems (Maruyama et al, 1986).

Point A is a reference point for cervical cancer brachytherapy 2 cm above the fornix and 2 cm lateral to the uterine tandem. The reference point is useful for specifying and analysing radiation dose given to the Stage IB tumour. Point A is also a useful point for comparing dosimetry used for cervical tumour therapy between different radiation centres. At the University of Kentucky, the treatment dose using Cs was 20–40 Gy at point A in a single implant session (Maruyama et al, 1989c); the dose for Cf was escalated from approximately 750 to 3000 cGy-equivalents (cGy-eq) at point A given in a single or two sessions (Maruyama et al, 1989a). The implant using Cf was usually performed at the start ("early") (Maruyama, 1979; Maruyama et al, 1980) but in some instances, especially in initial trials, was done after the start or at the completion of external-beam irradiation; the Cs was always implanted after the delivery of approximately 30–45 Gy of whole pelvis external beam irradiation (*i.e.* "delayed") (Maruyama & van Nagell, 1982). The Cs treated patient treated between 1975 and 1987 were used for this review (Maruyama et al, 1989c). The Cf schedule evolved based on studies showing that tumour regression was rapid after the early implant (Maruyama & Muir, 1982). The delayed Cs schedule is conventional in radiotherapy. In the Cf series, we reviewed cases where only Cf implant therapy was done, *i.e.* no mixed implants of Cf and Cs were included. The Cf treated patients were reported earlier (Maruyama et al, 1989a).

Exploratory surgery of the abdomen, pelvis and extrafascial hysterectomy, *i.e.* total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAHBSO) were done on all patients. The surgical methods have been reported in detail (van Nagell et al, 1986). Hysterectomy was carried out 4–6 weeks after the completion of radiotherapy.

Specimens were carefully studied; the uterus was opened laterally and fixed in 10% neutral Formalin (Maruyama et al, 1982). The entire uterus and cervix was divided radially into 12 segments and examined for residual disease. The vagina and parametria were also examined. Any evidence of tumour, either gross or microscopic, was designated as positive. Specimens were negative if there was no gross or microscopic tumour after thorough study. The pathologist was not advised of the treatment prior to analysis. All specimens were reviewed by pathologists of this institution using a single protocol for study.

The literature was used for worldwide comparative data on residual tumour following trials of pre-operative radiation followed by hysterectomy (Villasanta, 1968; Rampone et al, 1973; Churches et al, 1974; Surwit et al, 1975; Einhorn et al, 1980; Maruyama et al, 1980, 1985; Hansen, 1981; Perez & Kao, 1985; Perez et al, 1987). These are listed in Table I and the doses of radiation, radionuclide and dose rate used noted. Most of the literature experience is based on Ra-226 treatments, but that experience should be the same as with Cs. Most low dose rates (LDR) *i.e.* dose rates of about 50–60 cGy/h were as used at Paris, Manchester and the M.D. Anderson Hospital. Some centres used the moderate dose rate (MDR) methods of approximately 100 cGy/h advocated in the Stockholm method (Einhorn et al, 1980). All centres used surgery approximately 4–6 weeks following radiation. In some centres, whole-pelvis irradiation was added with some using both external and intracavitary therapy. Both external and intracavitary therapy are routinely performed at the University of Kentucky. The total dose was estimated to vary from 50–80 Gy at point A from all techniques used. The specimens showing residual tumour were plotted against dose and a dose–effect curve was constructed from the literature and our data. The University of Kentucky data are accurately determined for all components (neutrons or γ rays) and all isodose curves and loadings were optimized to avoid overdose to normal tissue and to deliver high doses to tumour (Maruyama et al, 1976).

All our patients were from this region and have been followed by regular follow-up examination or by information provided by the family, referring physicians or the state health department records.

Results

Tumour eradication from hysterectomy specimens

The endpoint of tumour eradication was used to assess tumour response to therapy using a direct histological or gross means of study (Maruyama et al, 1982). It was applied to this study using reported data of published studies for Cs, ^{226}Ra (Ra), ^{60}Co (Co), or Cf (Table I). Tumour may be microscopically present and evident on histological study or may be evident as gross residual pelvic tumour. Both were considered positive. Table I lists the literature data upon which this part of the study was based. The histopathology, tumour sizes and patient characteristics were similar for the Cs and Cf groups (Maruyama et al, 1988b, 1989a, c). Tumour therapy by external beam was very similar in both groups (Table II) but the intracavitary dose was different.

Analysis of neutron dose–response

Table II presents data from the patients treated with Cf with the observations related to the Cf intracavitary implant dose and to whole pelvis radiation dose. The external beam pelvis dose was not different in dose, dose per fraction or overall time and fraction number between Cf and Cs. The radiations from Cf are comprised of about $\frac{2}{3}$ neutrons and $\frac{1}{3}$ low dose rate photons at point A. Neutron dose at point A was calculated as a fraction of total dose. Data are detailed for the 1 × and 2 × implants and the data are plotted in Fig. 1. The 1 × implant produced a steeper dose–response curve compared to the 2 × implants. This demonstration of greater efficacy of fewer implants has been reported earlier (Maruyama et al, 1985c). It could be a result of decreased SLD repair, or to repopulation of surviving tumour cells following rapid regression of the killed tumour cells after the first implant. The D_{37} of the Cf (× 1) was 112 cGy and for Cf (× 2) was 230 cGy

Table I. Residual tumour in resected cervix cancers after pre-operative radiation for operable cancers

Author	Year	Tumour stage	Whole pelvis external beam dose (Gy)	Point A intracavitary dose	Number of patients	Positive specimens (%)	Radionuclide
Maruyama et al	1988b	I_B	43	21[b] Gy-eq	20	5	^{252}Cf
Maruyama et al	1988b	I_B	43	21 Gy (× 1)	44	35	^{137}Cs
Maruyama et al	1989c	I_B	43	21 Gy (× 1)	80	37	^{137}Cs
Perez and Kao	1985	I_B, II_A	20	6000 mgh[d] (× 1)	26	36	NS[a]
Perez et al	1987	I_B, II_A	20	65–70 Gy (× 2)	62	25	^{60}Co/^{137}Cs
Hansen	1981	I_B	43	42 Gy (× 2) MDR[c]	111	41	^{226}Ra
Einhorn et al	1980	I_B, II_A	+	50 Gy (× 2) MDR[c]	74	8	^{226}Ra
Surwit et al	1976	I_B	—	4000–4999 mgh[d]	58	33	^{226}Ra
Churches et al	1974	I_B	—	60 Gy (× 1)	427	24	^{226}Ra
Villasanta	1968	I_B	—	4500–5000 mgh[d]	56	23	^{226}Ra
Rampone et al	1971	I_B	—	57–63 Gy	573	13.4	^{226}Ra
				Total cases[e]	~ 1511	28 ± 10% (SD)	

[a] Not stated.

[b] cGy-equivalents.

[c] Moderate (Stockholm) dose rate.

[d] mgh given (cGy/mgh assumed to be ~ 1.0).

[e] Some patients overlap.

+ 50 Gy to parametria.

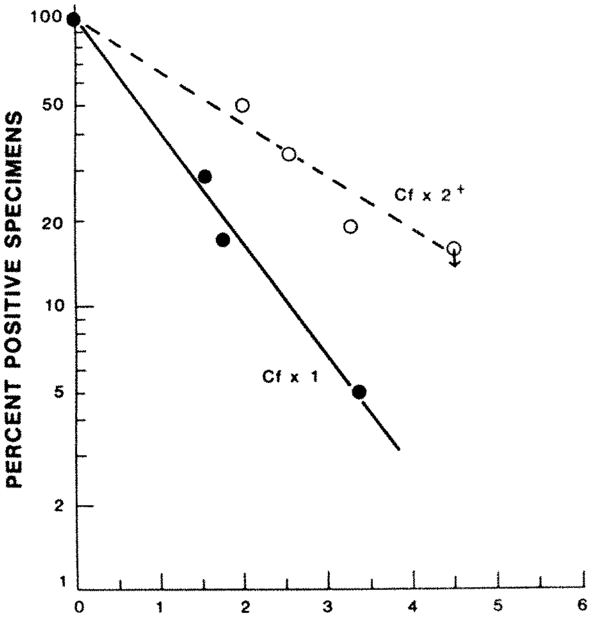

Figure 1. Dose–response graph for the percentage of positive specimens after radiosurgery and histological study after Cf-252 implant therapy ×1 (closed circles) or ×2 (open circles). D_{37} for ×1 was 112 cGy and for ×2 was 230 cGy. Slopes of curves were ×1, −0.8937 with $r=0.99$ and ×2, −0.4380 with $r=0.99$. These were significantly different ($p \leq 0.001$) by linear regression least squares fit. The two implants were done an average of 22.5±5.4 days apart.

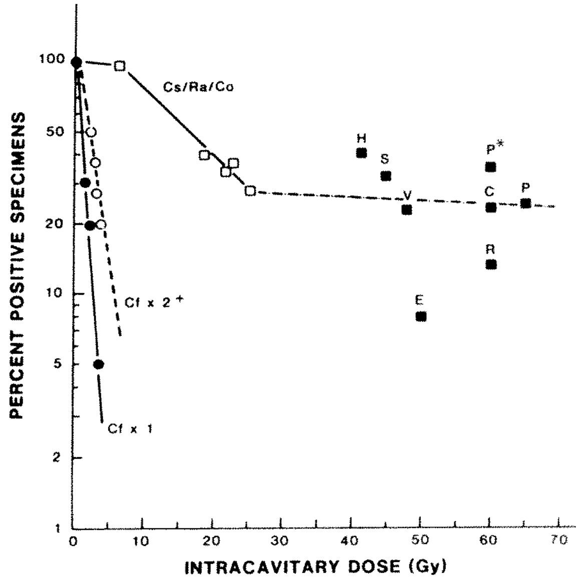

Figure 2. Dose–response curves for the percentage of positive specimens *versus* dose of neutrons or γ radiation. Closed circles are Cf ×1; open circles are Cf ×2. Open squares are point A dose in cGy from University of Kentucky experience. Closed squares are estimated point A dose and reported percentage positive specimens from literature (see Table I). Letters above squares denotes authors: H = Hansen (1981); S = Surwit et al (1975); P = Perez and Kao (1983) or Perez et al (1987); V = Villasanta (1968); C = Churches et al (1974); R = Rampone et al (1973); E = Einhorn et al (1980). In this study we assumed the RBE of Cs, Radium 226 and Cobalt 60 were 1.0 for high energy γ photon brachytherapy.

as shown in Fig. 1. The mean time interval between implants was 22.5±5.4 days. These data show the importance of size of dose of neutrons and number of treatment sessions in neutron therapy. They show that there was a decrease in efficacy by a factor of 2.04 for a fractionation time interval of ~22.5 days. This means that if two fractions are used, the dose must be doubled to achieve equivalent effect (*i.e.* the tumour clearance endpoint).

Photon dose response

We have reported elsewhere about the fraction of specimens showing tumour as a function of dose (Maruyama et al, 1989c). The data are plotted in Fig. 2 for our own results and the results from reported world-wide experiences (Table I). While our study used Cs, the bulk of the world studies reviewed used ^{226}Ra. The efficacy of ^{226}Ra and Cs are very similar and both should

Table II. Therapy details for ^{252}Cf implant ×1 and ×2 patients: external beam and implant dose

Number of procedures	Number of patients	Whole-pelvis radiation dose (Gy)	Number of fractions	Overall time (days)	Implant dose (cGy-eq)[b]	Neutron dose (cGy)
Cf ×1	22	44.9 (1.3)	24 (0.7)	36 (1.2)	1142±312[a] Range (831–2000)	177±47[a] (125–300)
Cf ×2	31	43.6 (0.5)	24 (0.3)	37 (0.7)	2008±451[a] Range (1209–3000)	298±71[a] (182–450)
Total	53					

( )Standard error.
[a]Standard deviation.
[b]cGy-eq value were based on a RBE assumed to be 6.0.

have RBE values of ~1.0. The curve for photon brachytherapy is plotted logarithmically and showed an initial threshold followed by a curve with two exponentially declining components. The initial region and data (open circles) are University of Kentucky observations where a single implant was prescribed as part of the pre-operative treatment regimen. The closed squares show data reported from worldwide experiences (total ~1500 patients). The data indicate an average residual tumour frequency of 28%. The data also shows a responsive group (to ~30 Gy) followed by a less responsive group to approximately 40–70 Gy at point A based on published data (Table I).

Cf neutron and photon comparison, and RBE

The RBE can be estimated from the dose to produce a 30% incidence of residual tumour in hysterectomy specimens by Cf or by Cs/^{226}Ra/^{60}Co. For a 1 × Cf implant, the RBE may be higher; the RBE may be reduced when given in two sessions. The data indicate the importance of the number of neutron implant sessions. We have stressed elsewhere that the size of the neutron dose per session (Maruyama et al, 1988a), the schedule (Maruyama et al, 1980), as well as treatment volume are all of great importance to outcome for high LET neutron therapy (Maruyama, 1988). The RBE was ~8.0 at low doses or multiple implants and may rise to ~16 with large dose single implants

Discussion

The advantages from the use of neutron therapy reflect the high RBE, a low oxygen enhancement ratio (Gray et al, 1983; Fowler, 1986), absence of cell age effects (Gragg et al, 1978), and limited repair of sublethal damage (SLD) or potentially lethal damage (PLD) (Gragg et al, 1977). The RBE of neutrons has been extensively studied using cells, rodents and a variety of large animals (Feola et al, 1986; Kal, 1986a) but there is little data for human tumours. In fact, few suitable endpoints exist in man except skin reaction (Stone, 1948; Sheline et al, 1971; Kal, 1986; Yamashita et al, 1986) complications in normal tissues (Cohen et al, 1985, 1989; Kal 1986b) tumour regression or regression rate (Feola et al, 1986; Parish et al, 1987; Maruyama et al, 1984). We have also studied survival time in animals (Maruyama et al, 1988a). Tumour eradication from bulky Stage IB cervical cancers treated with whole-pelvis radiation and either Cs or Cf intracavitary implants followed by surgery allowed an evaluation of the efficacy of Cs or Cf for tumour eradication. We have reported dose–response studies aimed to determine the frequency of tumour eradication from surgically resected, pathologically studied specimens (Maruyama et al, 1985c, 1988b, 1989a, c) and by tumour control studies. Such studies have been carried out for both Cs and Cf and allow an estimation of RBE based on radiation dose required to eradicate tumour. Californium emits both fast neutrons and γ rays and delivers a localized high LET radiation which is highly effective against the factors which constitute the major bases of radioresistance in tumours. For cervical cancer, the major factors for radioresistance are based on tumour bulk and hypoxia (Maruyama, 1984) as has been established by many studies.

The histological eradication of tumour from resected specimens was a method of study applied as a measure of neutron fractionation effect and to compare efficacy and specifically to provide data for estimating the RBE. The method used pre-operative radiation, an implant of Cf or Cs, followed 4–6 weeks later by TAHBSO and thorough histologic study of the specimen using a set study protocol. The positive and negative specimens offer a measure which reflects the efficacy of the therapeutic intracavitary radiation to eradicate tumour. The tumours studied were of a single stage, *i.e.* Stage IB bulky or barrel tumours, and the treatment radiation isodose curves adequately cover the tumour volume being studied (Maruyama et al, 1985a). The radiation doses delivered to the reference volume and point A dose were accurately evaluated in our studies using Cs and Cf and the endpoint used was common to both. The histological endpoint used may be superior to studies using tumour regression or complication frequency in normal tissues to estimate tumour RBE.

The present studies also allow the shape of the dose–response curves to be assessed. They support a one-hit inactivation of tumour by Cf neutrons (Maruyama, 1984). However, they also indicate a curvilinear dose–response curve for Cs following a multi-hit type of inactivation for low LET photon radiation. Photon radiations usually show a threshold at low doses with increasing response at higher doses. Our data with Cs and data from worldwide studies after pre-operative radioactive implant therapy have never reported total eradication of tumour using photon therapy. On the other hand, Cf produced 95% eradication of tumour from specimens, the highest value reported to date (Maruyama et al, 1988b). Reviews of residual tumour with implant doses between 40 Gy and 60 Gy of low dose-rate or moderate dose-rate radiation to 50–80 Gy (Table I) have reported an average of 28% positive specimens regardless of the dose used. Thus, tumour response to photons may reflect two differently responding cell populations present in cervical tumours. This radioresistance appears to be overcome by Cf neutrons, as was shown in our study (Fig. 2).

The present RBE value determined for cervical cancers is estimated to be about 8.0 at the 30% isoeffect level depending on number of implants performed. A single implant was more effective with a RBE ~16.0 but depended on size of dose and schedule. The 30% isoeffect level was used as a comparative endpoint against γ intracavitary therapy as residual tumour was noted in about 30% of specimens using γ-ray therapy. In our studies, using Cs irradiation plus 45 Gy of whole pelvis radiation, similar values were noted. Interestingly, Cs/Ra dose to 6000–8000 mgh levels or the use of moderate dose rate or low dose rate methods have not been shown to produce more negative specimens. Thus the suggestion that there are two sensitivities reflecting a more responsive (oxic ?) and a more resistant (hypoxic ?)

population is reasonable. This could also reflect differences in SLD or PLD repair or regeneration of rapidly growing or resting population of cells (Fowler, 1986) with less response to photons. For these resistant populations, Cf neutrons may greatly increase efficacy depending on dose per session, schedule, neutron dose and whether one or multiple implants are performed. Our results indicate a clear RBE advantage for Cf neutron brachytherapy for the therapy of bulky and radioresistant tumours. Such advantages cannot be overcome by photons based upon the established inherent dose–response characteristics of cells to photon radiation. In experimental animals, we noted similar complex dose–response curves, suggesting variable RBE values depending on size of dose delivered in tumours treated *in situ* in living mice bearing hypoxic and radioresistant tumour (Maruyama et al, 1988a).

In summary, the present study estimates an RBE for Cf neutrons based on the endpoint of tumour eradication from hysterectomy specimens of Stage IB bulky or barrel-shaped tumours. The data and dose response curves give insight into localized neutron effects for human tumours wherein radioresistance is based mainly on the hypoxia and bulky size. For these and similar tumours, where local failure and radioresistance are a problem, Cf offers a method for improving local tumour control. Combined with large field photon radiation to 50–60 Gy, tumour cure was found to be easily achieved even in the earliest feasibility trials followed to 10 years (Maruyama et al, 1989b). The complication rate using the Kentucky protocol for treatment was ~5% (*i.e.* fistulae and bowel obstruction) but was of the same frequency or severity as that observed with Cs therapy. Finally, concerns about late effects of neutron therapy, *e.g.* delayed tumours such as leukemia or lymphoma, and aplastic anemia in the cured long-term surviving patients have not been observed in our experience with 7–14+ year cured patients. The present study offers RBE data useful for the treatment of tumours. They indicate that an up-front, localized Cf treatment of 375–500 neutron cGy (dose and effects dependent on dose rate used) followed by 50–60 Gy of low LET whole-pelvis large field irradiation should prove effective for local control and cure of these tumours. The present data suggest that true RBE may be a complex value depending on Cf schedule used, dose per session, number of sessions, tumour size and possibly histologic pattern being treated. Cf should be as effective as current lengthy photon treatment methods and more effective than multiple sessions of acute high-dose photon radiation therapy treatments. This should improve tumour control, reduce expense and time with few late complications. Further trials are clearly warranted and the use of remote afterloading machines will greatly facilitate the trials (Maruyama et al, 1986; Yamashita et al, 1986).

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References

Bush, R. S., Jenkins, R. D., Allt, W. E., Beale, F. A., Bean, H., Dembo, A. J. & Pringle, J. F., 1978. Definitive evidence for hypoxic cells influencing cure in cancer therapy. *British Journal of Cancer (Suppl.), 37*, 302–306.

Coffey, C. W., Yoneda, J., Beach, J. L. & Maruyama, Y., 1986. Methods for Cf-252 cervix cancer therapy and treatment planning for GYN malignancies in Lexington. *Nuclear Science Applications, 2*, 485–496.

Churches, C. K., Kurtle, G. R. & Johnson, B., 1974. Treatment of carcinoma of the cervix by combination of irradiation and surgery. *American Journal of Obstetrics and Gynecology, 118*, 1033–1040.

Cohen, L., Schultheis, T. E., Hendrickson, F. R., Marsell, J., Saroja, K. R. & Lennox, A., 1989. Normal tissue reactions and complications following high-energy neutron beam therapy: I. Crude response rates. *International Journal of Radiation Oncology, Biology, Physics, 16*, 73–78.

Cohen, L., Tattahem, R. X., Marsell, J., Yalawarthi, S. D., Hendrickson, F. R. & Awschalom, M., 1985. Tolerance of the human spinal cord to high energy p(66) Be(49) neutrons. *International Journal of Radiation Oncology, Biology, Physics, 11*, 743–749.

Durrance, F. Y., Fletcher, G. H. & Rutledge, F. N., 1969. Analysis of central recurrent diseases in Stage I and II squamous cell carcinomas of the cervix on intact uterus. *American Journal of Roentgenology, 106*, 831–838.

Einhorn, H., Bydemm, M. & Sjoberg, B., 1980. Combined radiation and surgical treatment for carcinoma of the uterine cervix. *Cancer, 45*, 720–723.

Evans, J. C. & Bergsjo, P., 1965. The influence of anemia on the results of radiotherapy in carcinoma of the cervix. *Radiology, 84*, 709–716.

Feola, J. M., Maruyama, Y. & Beach, J. L., 1986. Tumor and normal tissue radiobiology for Cf-252 neutron therapy. *Nuclear Science Applications, 2*, 327–343.

Feola, J. M., Nava, C. A. & Maruyama, Y., 1982. Biological effects of Cf-252 neutrons at low dose rates. *International Journal of Radiation Biology, 41*, 33–36.

Fowler, J. F., 1986. Neutrons for radiotherapy of resistant tumors: Interaction with low LET. *Nuclear Science Applications, 2*, 221–234.

Gragg, R. L., Humphrey, R. M. & Meyn, R. E., 1977. The response of Chinese hamster ovary cells to fast-neutron radiotherapy beams. II. Sublethal and potentially lethal damage recovery capabilities. *Radiation Research, 71*, 461–470.

Gragg, R. L., Humphrey, R. M., Thames, H. D. Jr & Meyn, R. E., 1978. The response of Chinese hamster ovary cells to fast-neutron radiotherapy beams. II. Variation in relative biological effectiveness with position in the cell cycle. *Radiation Research, 76*, 283–291.

Gray, L. H., Conger, A. D., Ebert, M., Horney, S. & Scott, O. C. A., 1953. The concentration of oxygen dissolved in tissues at the time of irradiation as a factor in radiotherapy. *British Journal of Radiology, 26*, 638–648.

Hansen, M. K., 1981. Surgical and combination therapy of cancer of the cervix uterine Stage IB & IIA. *Gynecologic Oncology 11*, 275–287.

Hardt, N., van Nagell, J. R., Hanson, M., Donaldson, E., Yoneda, J. & Maruyama, Y., 1982. Radiation induced tumor regression as a prognostic factor with invasive cervical cancer. *Cancer, 49*, 35–39.

Kal, H. B., 1986a. Review of RBE and OER values for Cf-neutrons. *Nuclear Science Applications, 2,* 303–316.

—— 1986b. Complications of Cf-252 radiotherapy: review of reported experiences. *Nuclear Science Applications, 2,* 409–418.

Kottmeier, H. L. (Ed.), 1979. *Annual report on the results of treatment of carcinoma of the uterus, vagina, and ovary, Vol. 17.* (International Federation of Gynecology and Obstetrics, Stockholm), pp. 13–111.

Maor, M., Gillespie, B. W., Peters, L. J., Wambesie, A., Griffin, T. W., Thomas, F. J., Cohen, L., Conner, N. & Gardner, P., 1988. Neutron therapy in cervical cancer: results of a phase III RTOG study. *International Journal of Radiation Oncology, Biology, Physics, 14,* 885–891.

Maruyama, Y., 1979. Rapid clearance of advanced pelvic carcinoma by californium-252 therapy. *Radiology, 133,* 472–475.

—— 1984. Cf-252 neutron brachytherapy: advance for bulky localized cancer therapy. *Nuclear Science Applications, 1,* 677–748.

—— 1988. Cf-252 new radioisotope for neutron therapy of bulky cervix, uterus, and other cancers for developing nations. In *Selected Topics in Physics of Radiotherapy and Imaging.* Ed. by U. Madhvanth, K. S. Parthasarathy & T. V. Venkateswavan (Tata–McGraw Hill, New Delhi), pp. 151–179.

Maruyama, Y. & Muir, W., 1982. Human cervical cancer clearance after ^{252}Cf neutron brachytherapy vs. conventional photon brachytherapy. *American Journal of Clinical Oncology (CCT), 7,* 347–352.

Maruyama, Y. & van Nagell, J. R., 1982. Radiation therapy for cervical cancer. In *Modern Concepts of Gynecology Oncology.* Ed. by J. R. van Nagell & H. R. K. Barber. (PSG–Wright, Boston), pp. 91–158.

Maruyama, Y., van Nagell, J. R., Wrede, D. F., Coffey, C. & Utley, J. F., 1976. Approaches to optimization of dose in radiation therapy of cervix carcinoma. *Radiology, 20,* 389–398.

Maruyama, Y., Beach, L. J. & Feola, J. M., 1980. Scheduling of hypoxic tumor therapy using neutron brachytherapy. *Radiology, 137,* 775–781.

Maruyama, Y., Yoneda, J., van Nagell, J. R., Donaldson, E., Hanson, M., Powell, D. & Muir, W., 1982. Tumor regression and histologic clearance after neutron brachytherapy for bulky localization cervical carcinoma. *Cancer, 50,* 2802–2809.

Maruyama, Y., Feola, J. M. & Beach, L. J., 1983. A tumor/normal tissue advantage for low dose rate neutron brachytherapy. *International Journal of Radiation Oncology, Biology, Physics, 9,* 1715–1721.

Maruyama, Y., Feola, J. M. & Beach, L. J., 1984. Hela cell tumor response to Co-60, Cs-137, Cf-252 radiations and Cis-platin chemotherapy in nude mice. *Cancer, 54,* 247–252.

Maruyama, Y., Beach, L. J., Hazle, J., Ashtari, M. & Schroy, C. B., 1985a. Therapeutic dosimetry for Cf-252 neutron brachytherapy of pelvic cancer. *International Journal of Radiation Oncology, Biology, Physics, 11,* 927–955.

Maruyama, Y., Kryscio, R., van Nagell, J. R., Yoneda, J., Donaldson, E., Hanson, M., Feola, J. M., Martin, A. & Parker, C., 1985b. Clinical trial of ^{252}Cf neutron brachytherapy vs conventional radiotherapy for advanced cervical cancer. *International Journal of Radiation Oncology, Biology, Physics, 11,* 1475–1482.

Maruyama, Y., van Nagell, J. R., Feola, J. M., Yoneda, J., Donaldson, E., Gallion, H., Rowley, K. & Powell, D., 1985c. Specimen histology after one or two preoperative Cf-252 implants for bulky stage IB cervical cancer. *International Journal of Radiation Oncology, Biology, Physics, 13,* 1473–1478.

—— 1985d. Neutron brachytherapy is better than conventional radiotherapy in advanced cervical cancer. *Lancet, i,* 1120–1121.

Maruyama, Y., Beach, L. J. & Feola, J. M., 1986. Cf-252 neutron brachytherapy and fast neutron beam therapy. *Nuclear Science Applications, 2,* 187–826.

Maruyama, Y., van Nagell, J. R., Yoneda, J., Donaldson, E., Gallion, H., Rowley, K. & Kryscio, R., 1987. Phase I/II clinical trial of californium-252 treatment of Stage IB carcinoma of the cervix. *Cancer, 59,* 1500–1505.

Maruyama, Y., Darwazeh, N. & Magura, C., 1988a. Increased ^{252}Cf therapeutic advantage for advanced murine lymphoma (LSA) growing *in vivo. British Journal of Radiology, 61,* 312–316.

Maruyama, Y., van Nagell, J. R., Yoneda, J., Donaldson, E., Gallion, H., Higgins, R., Powell, D. & Kryscio, R., 1988b. Efficacy of brachytherapy with Californium-252 neutrons versus Cs-137 photon for eradication of bulky localized cervical cancer: single institutional study. *The Journal of the National Cancer Institutes 80,* 501–506.

Maruyama, Y., van Nagell, J. R., Yoneda, J., Donaldson, E., Martin, A., Wilson, L. C., Feola, J. M., 1988c. Ten year cures of gynecologic tumors with Cf-252 neutron brachytherapy. *Radiology, 169,* 238.

Maruyama, Y., van Nagell, J. R., Yoneda, J., Donaldson, E., Gallion, H., Higgins, R., Powell, D., Turner, C. & Kryscio, R., 1989a. Dose response for Cf-252 neutron brachytherapy by histological eradication of bulky stage IB cervical tumors. *EndoCurieTherHypertherOncol, 5,* 111–120.

—— 1989b. Cure of cervical cancer using Cf-252 neutron brachytherapy. *Strahlentherapie Onkologie* (in press).

Maruyama, Y., van Nagell, J. R., Yoneda, J., Donaldson, E., Gallion, H., Powell, D., Kryscio, R., Berner, B., 1989c. Dose–response and failure pattern for bulky or barrel-shaped Stage IB cervical cancer treated by combined photon irradiation and extrafascial hysterectomy. *Cancer, 63,* 70–76.

Parish, S., Feola, J. & Maruyama, Y., 1987. EMT6 tumor response to Cobalt-60, Cesium-137 and Californium-252 radiation in BALB c mice. *EndoCurieTherHypertherOncol, 3,* 3–9.

Perez, C. A. & Kao, S. M., 1985. Radiation therapy alone or combined with surgery in the treatment of bulky-shaped carcinoma of the uterine cervix (Stage IB, IIA, IIB). *International Journal of Radiation Oncology, Biology, Physics, 11,* 1903–1909.

Perez, C. A., Camel, H. M. & Kao, M. S., 1987. Randomized study of preoperative radiation and surgery or irradiation alone in the treatment of stage IB and IIA carcinoma of the uterine cervix: final report. *Gynecologic Oncology, 27,* 129–140.

Rampone, J. F., Klem, V. & Kolstad, P., 1973. Combined treatment of Stage IB carcinoma of the cervix. *Obstetrics and Gynecology, 41,* 163–167.

Sheline, G. E., Phillips, T. L., Field, S. B., Brennan, J. T. & Raventos, A., 1971. Effects of fast neutrons in human skin. *American Journal of Rontgenology, 111,* 31–41.

Stoddard, D. H., 1986. Historical review of Californium-252 discovery and development. *Nuclear Science Applications, 2,* 189–199.

Stone, R. S., 1948. Neutron therapy and specific ionization. *American Journal of Rontgenology, 59,* 771–785.

Surwit, E., Fowler, W. C., Palumbo, L., Koch, G. & Gjertsen, W., 1975. Radical hysterectomy with or without preoperative radium for Stage IB squamous cell carcinoma of the cervix. *Obstetrics and Gynecology, 48,* 130–133.

VALLEJO, A., HILARIS, B. & ANDERSON, L. L., 1977. ^{252}Cf for interstital implantation: a clinical study at Memorial Hospital. *International Journal of Radiation Oncology, Biology, Physics, 2,* 731–737.

VAN NAGELL, J. R., MARUYAMA, Y., YONEDA, J., DONALDSON, E. S., HANSON, M., GALLION, H. H., YONEDAS, POWELL, D. E. & KRYSCIO, R. J., 1986. Phase II clinical trial using californium 252 fast neutron brachytherapy, external pelvic radiation and extrafascial hysterectomy in the treatment for bulky, barrel-shaped, Stage IB cervical cancer. *Cancer, 57,* 1918–1922.

VILLASANTA, U., 1968. Combined radium therapy and radical hysterectomy with pelvic lymphadenopathy in treatment of invasive cancer of the cervix. *Obstetrics and Gynecology, 32,* 6–10.

WATSON, E. R., HALAN, K. E., DISCHE, S., SAUNDERS, M. I., CADE, I. S., MCIWEN, J. B., WIERNIK, G., PERRINS, D. J. D. & SUTHERLAND, I., 1978. Hyperbaric oxygen and radiotherapy: a Medical Research Council trial in carcinoma of the cervix. *British Journal of Radiology, 51,* 879–887.

YAMASHITA, H., HASHIMOTO, S., WADA, M. & DOKIYA, T., 1986. Fast neutron therapy with high intensity of Cf-252 source by remotely controlled afterloading and clinical experiences in the treatment of gynecological cancers. *Nuclear Science Applications, 2,* 453–466.

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The effect of secondary electron spread on the penumbra in high energy photon beam therapy

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Abstract. In photon beam therapy, the geometric penumbra width is determined by the source-size and the collimator design. The width of the physical (*i.e.* dosimetric) penumbra involves an additional contribution from secondary electron spread. Using a suitably defined measure of penumbra width, the separate widths due to photons and secondary electrons are additive in quadrature. Secondary electron spread functions were measured using photographic dosimetry for ^{60}Co γ rays and for 4, 8 and 16 MV X rays. The results suggest that, under typical treatment conditions, secondary electron spread may be the predominant contributor to the penumbra at effective generating voltages exceeding 10 MV. The implications for selection of beam energy in precision small-field radiotherapy are discussed briefly.

Radiotherapeutic significance of the penumbra

A basic tenet of external beam radiotherapy planning is to fit the target volume with a relatively high and uniform dose region whilst minimizing the irradiation of neighbouring healthy tissues. This is particularly difficult to achieve when critically radiosensitive organs (*e.g.* spinal cord) lie adjacent to the target volume. Ideally, in these circumstances, a point source is required, since this gives rise to minimal geometric penumbra. However, since all practical sources have finite dimensions, radiotherapists have had to take account of the penumbra when planning the treatment and particularly in specifying the appropriate field size.

Technical aspects of beam definition

In low and medium-voltage therapy, the focal spot size is usually such that the penumbra width can be adequately controlled by good applicator design. For this purpose, relatively imprecise knowledge of the source-size is sufficient and the penumbra can often be regarded as a narrow and insignificant zone of dosimetric uncertainty.

The advent of higher energy telecurietherapy using cobalt 60 and caesium 137 re-opened the question of penumbra reduction. Because of their weight, applicators are generally impractical for this type of therapy, and field definition was achieved by collimating jaws mounted in the radiation head at some distance from the patient in order to utilize the skin-sparing effect. The overall design strategy became to minimize the source-size, and in turn the geometric penumbra, by maximizing the specific activity of the radioactive source.

Secondary electron spread

Quite apart from source-size effects, it is apparent that the lateral spread of secondary electrons must also contribute to the penumbra (*e.g.* Day & Farmer, 1958; Adams, 1964; Dutreix et al, 1965; Roesch, 1968). As expected, such spread becomes more important the higher the energy (Bagne, 1980; Sasane & Iyer, 1981; Young & Kornelsen, 1983; Dawson et al, 1984). For photon energies up to about 1 MeV, the secondary electron range may be considered "negligible" and it is reasonable to assume that, except in the surface build-up zone, virtually electron equilibrium conditions prevail with no superficial build-up of dose and sharp cut-off at the beam edge. However, at higher photon energies, the transport of secondary electrons contributes significantly to the overall pattern of absorbed dose, particularly near the edge of the photon beam. It has been pointed out that because of the increased secondary electron range, the extent both of the longitudinal build-up zone and of the lateral spread are increased in low density materials *e.g.* lung tissue (Kornelsen & Young, 1982; Mackie et al, 1985b).

Quantification of the penumbra

There is evidently a need to quantify the dose distribution in the penumbra, especially with higher energy photons, taking account of the lack of secondary electron equilibrium. In general, it is useful to distinguish between the physical (*i.e.* dosimetric) and the geometric penumbra (ICRU, 1976). A complete analysis must consider the combined effects of all the various contributory processes, recognizing their differing dependence on radiation quality, field-size, source-distance and depth.

Many authors have published experimental measurements of high energy beam profiles. The published information is almost always graphical and is necessarily confined to specific field sizes and depths. The results represent the overall effect of the various spread processes and there is little information about the secondary electron spread function as such. Mackie et al (1985a) compared measured and calculated dose profiles for 10 × 10 cm and 30 × 30 cm fields irradiated with

15 MV X rays. The calculations included secondary electron spread and photon scatter but not geometrical penumbra. Dutreix et al (1965) have described photographic measurements of the three-dimensional "influence function" (Roesch, 1958) for 20 MV X rays. Shapiro et al (1955) report related results for small X-ray fields irradiated with 22.5 MV X-ray beams. In general, these results confirm the expectation that the lateral spread of absorbed dose will be less than the secondary electron range as indicated by the depth of maximum dose.

The differential pencil beam (DPB) model

There has been considerable progress towards the goal of deriving all types of dose distribution from fundamental physical parameters (Petti et al, 1983). The method is based on the Monte Carlo derivation of a convolution kernel (Ford & Nelson, 1978), which in principle allows calculation of the absorbed dose distribution for any pattern of incident photon fluence, and for heterogeneous body tissues (Boyer & Mok, 1986; Petti et al, 1987). The lateral spread of secondary electrons is allowed for, although not rigorously. Mohan & Chui (1985) give calculated point-spread functions and beam profile predictions for ^{60}Co γ rays and 10 MeV photons. In view of the inherent theoretical simplifications and idealizations of the DPB model, Chui & Mohan (1988) advocate extraction of the dose kernel by deconvolution of empirically measured data.

Purpose of the present paper

There appears to be a place for further experimental measurements of secondary electron spread, both in their own right and also for comparison with theoretically derived results.

The aims of the present work are:

(i) to indicate how functions describing the secondary electron spread can be derived experimentally with adequate accuracy for a range of radiation qualities;
(ii) to present results for ^{60}Co γ rays and for 4, 8 and 16 MV X rays;
(iii) to consider briefly the relative contributions to the penumbra of secondary electron spread and other processes, and the way in which they combine;
(iv) to outline the implications for selection of beam energy in clinical radiotherapy.

Theory

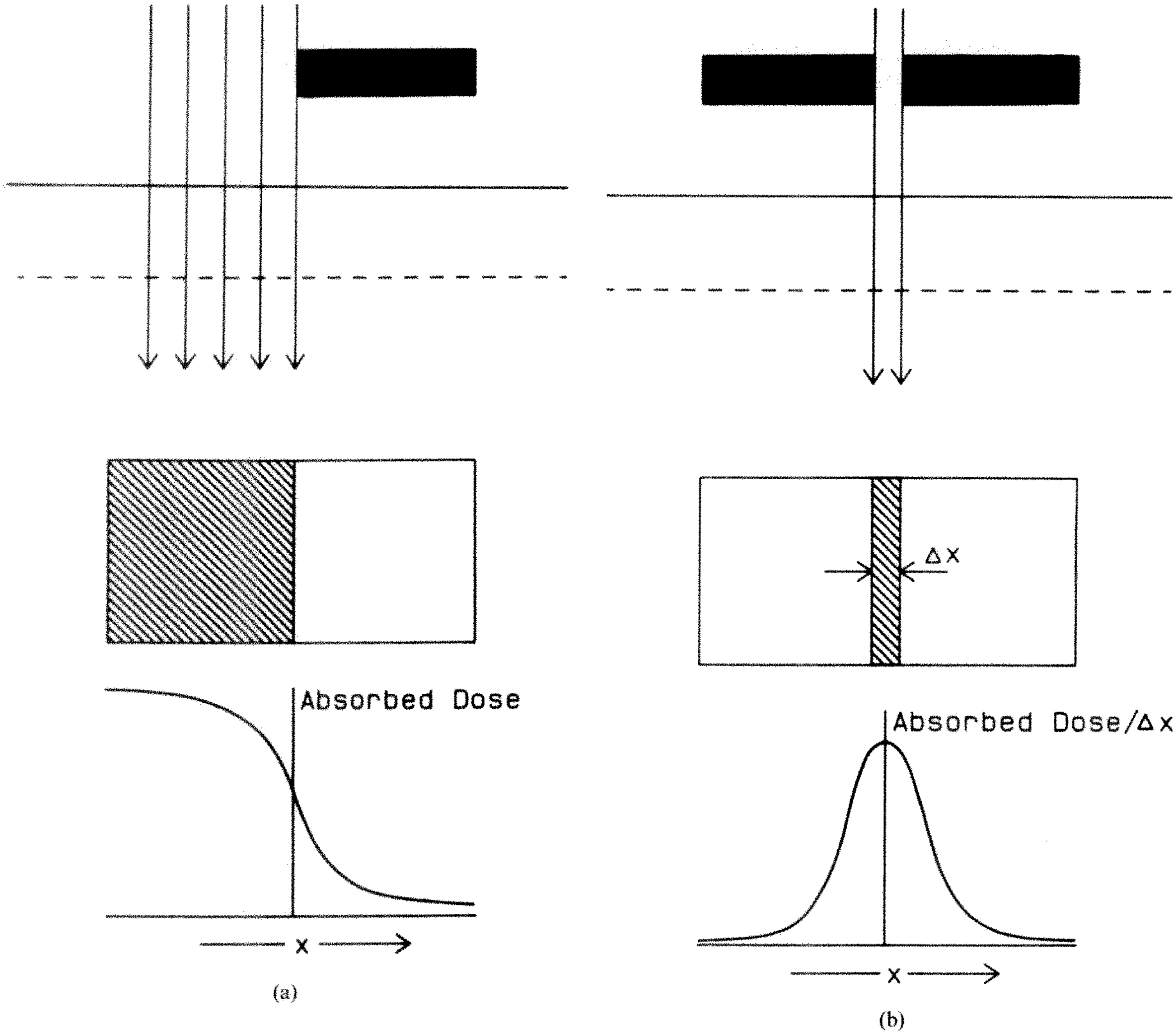
The rapid fall-off in absorbed dose at the edges of photon beams is largely, though not entirely, a result of the cut-off of primary fluence by the collimator. The dose rising from photon scattering in the phantom also decreases towards the edge of the beam and thereby makes a contribution to the physical penumbra (Haywood et al, 1979; Sutcliffe, 1980). This contribution is relatively small and, moreover, it is a function of both field size and depth. In what follows, we shall consider the penumbra arising from the primary photons only. This approach recognizes the marked physical differences between the dose distribution patterns of the primary and scattered photons and is compatible with established procedures for separate calculation of the primary and scatter doses (Cunningham, 1972; Mohan & Chui, 1985; Bjarngard & Cunningham, 1986).

The unsharpness of beam definition, including that resulting from the lateral spread of secondary electrons, is closely analogous to the unsharpness that occurs in imaging systems (Rossmann, 1969). The resulting distribution of absorbed dose may be described in terms of the edge-spread function (ESF), line-spread function (LSF) or point-spread function (PSF) (Fig. 1). In addition the modulation transfer function (MTF) may have important analytical and computational advantages. It is worth emphasizing that the above four functions are simply different ways of expressing the same physical information, and that there are precise mathematical relationships between them. Their formulation is considerably simplified when, as in this case, there is angular symmetry about the line of travel of the photons.

Radiotherapists are primarily interested in the penumbra width and in the shape of the ESF. If the spread is to be quantified by a single number, there are fundamental advantages in using a line-spread coefficient analogous to the standard deviation in statistics (Doi & Rossmann, 1975; Day, 1976). The particular merit of this coefficient is that, when there are several contributory processes, their individual spread coefficients combine according to a definite additivity rule, namely they are *additive in quadrature*. This conclusion holds whenever the individual processes are in a convolutional relationship *e.g.* when the geometric spread of the primary photons due to source-size (and collimator design) interacts with the inherent secondary electron spread.

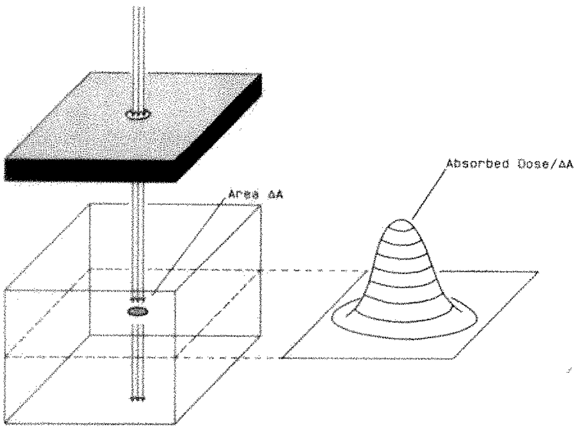
For practical purposes it is convenient to define the *nominal penumbra width* or *nominal overall spread* as a distance equal to four times the spread coefficient. This definition corresponds to the conventional statement of statistical confidence limits as "±2 standard deviations". Moreover, it is identical with the actual overall penumbra width with an ideal uniform disc source. Obviously nominal penumbra widths are additive in quadrature exactly like the basic spread coefficients. It should be noted that, in practice, it is virtually impossible to determine a definite overall width by direct measurement because the spread functions approach their extreme values asymptotically. As an alternative, many experimenters have noted the virtually linear variation of dose at the centre of the penumbra. This can be used as the basis for an *extrapolated penumbra width*; *e.g.* we have extrapolated linearly to 0% and 100% from the 20% and 80% points to give an extrapolated width equal to the 20–80% distance divided by 0.6.

In general, a full specification of the penumbra requires a complete statement of one or other of the ESF, LSF *etc.*, taking account not only of its width but also of its shape. When there is one predominant spread process the additivity rule implies that this process will



(a)

(b)



(c)

Figure 1. (a) The edge-spread function, (b) the line-spread function and (c) the point-spread function.

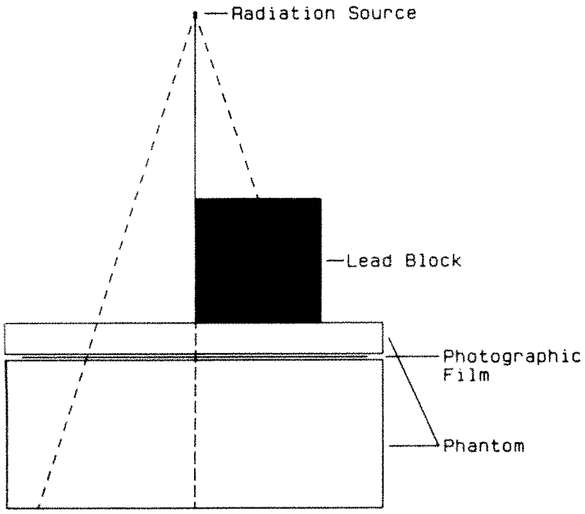


Figure 2. The experimental set-up.

practically determine the combined spread coefficient. The convolutional relationship means that it will also largely determine the shape of the spread function. If, however, there are two or more comparable spread processes, theory suggests that their combined spread function will approximate to the Gaussian form.

Experimental method

The ESF was measured by placing a machined lead block on a water-equivalent phantom and aligning its edge as accurately as possible with the central ray of the photon beam (Fig. 2). In general, the technique resembles that used by Mackie et al (1985a). The beam size was made large enough to ensure full lateral build-up in the absence of the block and to avoid interference from the contralateral penumbra. The source-distance during irradiation was made fairly long (1.5–2 m) so as to minimize the geometrical spread. Photographic dosimetry was used to record the edge-spread function at the peak depth.

Corrections were applied for:

(i) non-linearity of the photographic characteristic curve;
(ii) optical spread in the scanning densitometer;
(iii) penetration of photons through the lead block;
(iv) absorbed dose due to photons scattered in the phantom.

The spread function thus determined is that resulting from the *secondary electrons projected by the primary photons* from a slab of thickness equal to the depth of maximum dose. There is also a contribution from secondary electrons backscattered from the layer immediately beyond the depth of maximum dose. All spread functions are normalized to give unit (or 100%) absorbed dose when there is full lateral build-up of secondary electrons.

The LSF was obtained from the ESF by differentiation. The methods of Jones (1958) and Marchand (1964, 1965) were then used to derive the PSF. In general, the LSFs could be closely approximated by double exponential functions, from which the spread coefficients could be readily calculated.

Results

Typical measured ESFs, incorporating the four corrections mentioned above, are shown in Fig. 3. The agreement with the expected symmetry about the 50% point is reasonable, bearing in mind that the photon beam is not necessarily flat to better than 1%. The measurements could be fitted by

$$\mathrm{ESF}(x) = \mathrm{A}e^{\alpha x} + \mathrm{B}e^{\beta x} \ (x \text{ negative})$$

$$\mathrm{ESF}(x) = 1 - \mathrm{A}e^{-\alpha x} - \mathrm{B}e^{-\beta x} \ (x \text{ positive})$$

where $x =$ distance from edge of beam *i.e.* centre of penumbra and $\mathrm{A}+\mathrm{B} = 0.5$. A, B, α, and β are constants for a particular radiation quality (see Table I).

The line-spread function is

$$\mathrm{LSF}(x) = \mathrm{A}\alpha e^{-\alpha|x|} + \mathrm{B}\beta e^{-\beta|x|}$$

and the line-spread coefficient, S, is given by

$$S = 2\sqrt{\frac{\mathrm{A}}{\alpha^2} + \frac{\mathrm{B}}{\beta^2}}.$$

The nominal overall spread is equal to $4S$. For comparison, the extrapolated overall spreads, based on the 20% and 80% edge-spread values, are included in Table I. Note that these spread values are those resulting from secondary electrons alone.

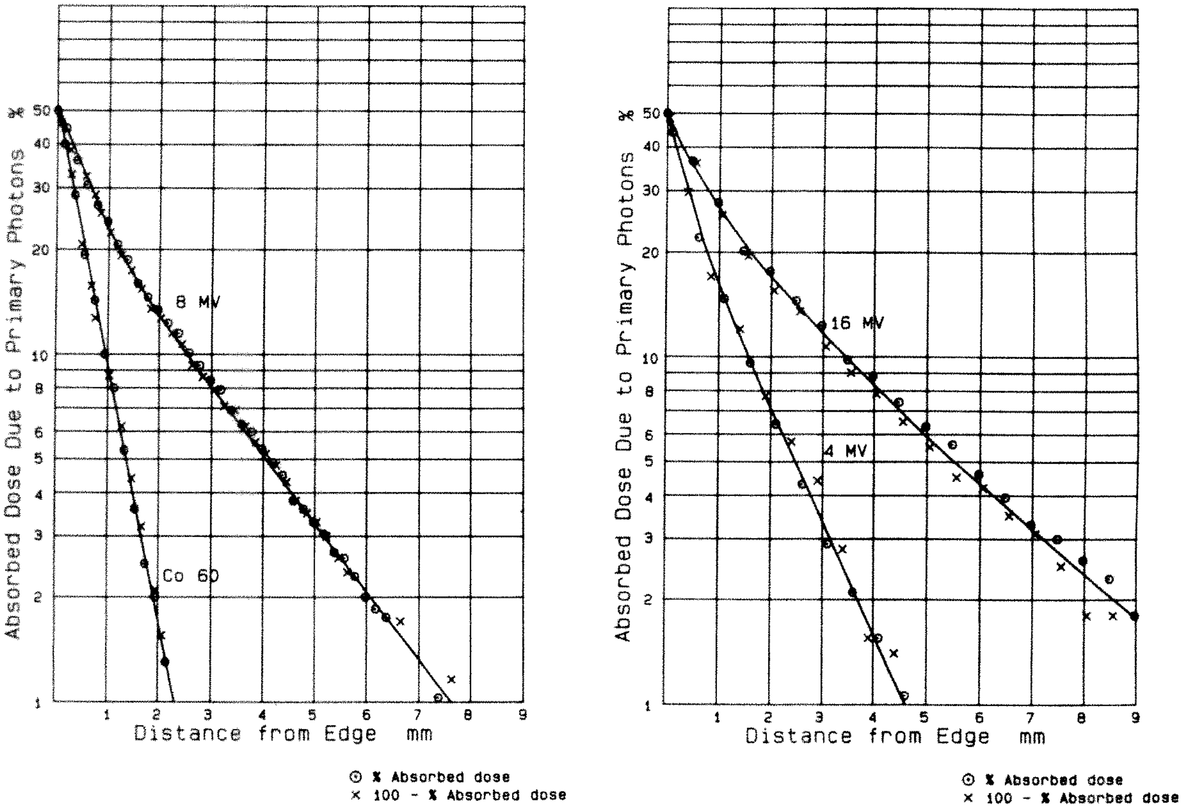
The corresponding LSFs and PSFs, for each of the radiation qualities, are shown graphically in Fig. 4.

Discussion

Inspection of Table I and Fig. 4 shows that the secondary electron spread increases as expected with the photon energy. As a rule of thumb, the nominal overall spread is roughly equal to half the electron range as represented by the depth of maximum dose. The estimated 25–75% penumbra widths of Haywood et al (1979) appear to be generally compatible with our extrapolated widths. However, although the extrapolated penumbra width may well be of practical convenience as a starting point for specification of the penumbra, it is apparent from the table that it may considerably underestimate the nominal overall width.

The main other process contributing to the penumbra width is the source-size effect. In the UK, cobalt 60 sources are usually 17 mm in diameter and the design of collimation systems is typically such that the geometrical nominal penumbra width is about 20 mm. By comparison, the nominal secondary electron spread of 3 mm is negligible. If penumbra trimmers are used, the geometrical spread can be reduced to about 6 mm, which would still considerably outweigh the secondary electron spread. The same considerations apply *a fortiori* to lower energy sources such as caesium 137.

With linear accelerators the focal spot size is usually less than 5 mm, and considerably smaller sizes have



(a) (b)

Figure 3. (a) Measured edge-spread functions for Cobalt 60 γ rays and 8 MV X rays, (b) measured edge-spread functions for 4 MV and 16 MV X rays. Note that points are plotted for absorbed doses of 0–50% (circles) and 50–100% (crosses).

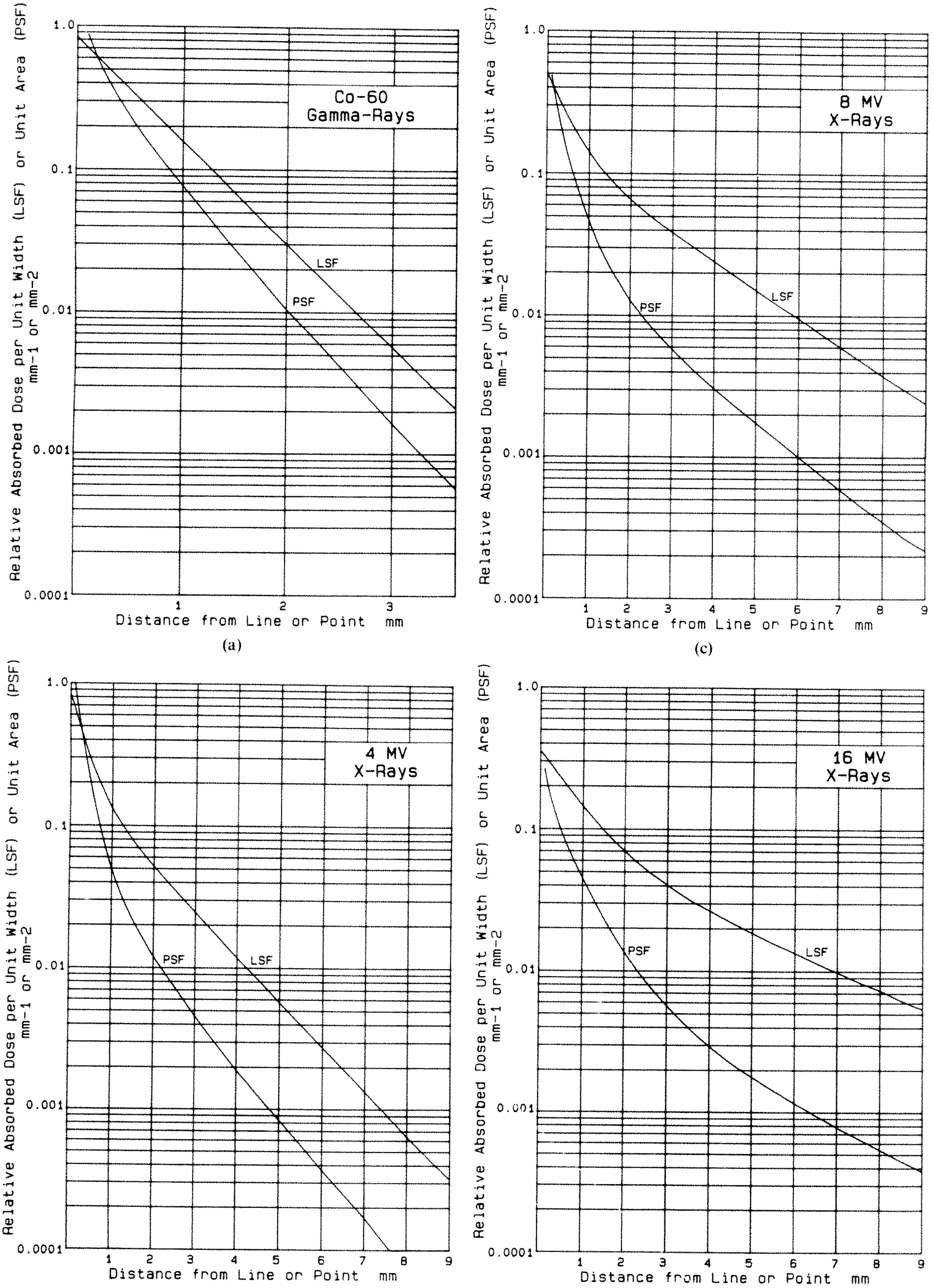
been reported for betatrons and microtrons. The design of beam-defining systems is such that the geometrical penumbra width should be similar to the focal spot size. Beam profile measurements however indicate typical penumbra widths of 10–20 mm. It is evident that source-size effects cannot fully explain these results.

The nominal penumbra widths given in Table I show that secondary electron spread will contribute significantly to the overall penumbra size. Indeed, for X rays generated above about 10 MV, it may well become the predominant spread process. This conclusion is in essential agreement with the theoretical finding of Mohan & Chui (1985) that, for 15 MV photons, the contribution of secondary electrons to the formation of the beam penumbra is of the same order of magnitude as the other factors combined. It is of interest that

Table I. Parameters of secondary electron spread function for various photon energies

Radiation type	d_{80} (cm)	d_p (cm)	Parameters of ESF				Line-spread coefficient (mm)	Overall spread^a	
			A	α (mm^{-1})	B	β (mm^{-1})		Nominal (mm)	Extrapolated (mm)
Cobalt 60	—	0.5	0.50	1.66	—	—	0.85	3.4	1.8
4 MV	5.9	1.0	0.30	0.73	0.20	3.20	1.53	6.1	2.4
8 MV	7.4	2.0	0.325	0.46	0.175	2.04	2.51	10.0	4.1
16 MV	9.1	3.0	0.265	0.30	0.235	1.18	3.53	14.1	5.3

d_{80} = depth for 80% depth dose in 10 × 10 cm field at 100 cm source–surface distance.
d_p = depth of maximum dose.
The extrapolated overall spread is equal to the 20% to 80% edge spread distance divided by 0.6.
^{a}Secondary electrons only.



(a) (c)

(b) (d)

Figure 4. Line-spread function and point-spread function. (a) Cobalt 60 γ rays, (b) 4 MV X rays, (c) 8 MV X rays and (d) 16 MV X rays. For (a) to (d), absorbed doses are normalized to unity for full lateral build-up of secondary electrons.

Cunningham et al (1972) describe the penumbra using a PSF of the single exponential type (*cf.* Fig. 4). Their usage is not precisely comparable with our finding because their function describes the convolution of the geometric penumbra with the secondary electron spread function, whereas our expression describes the secondary electron spread function alone.

In applying our data to specific X-ray generators it should be noted that the geometric contribution to the penumbra increases with distance from the collimating aperture, whereas the secondary electron contribution remains the same. This must be taken into account when assessing the width and also the "shape" of the penumbra at various depths.

All our measurements were made at the depth of maximum dose. Since the primary dose at any point is unaffected by events occurring further away than the secondary electron range, and beam-hardening effects are not important, we expect our results to be applicable to the primary component of the absorbed dose at any depth.

Conclusions

Although secondary electron spread is probably not a practically important contributor to the penumbra at generating voltages below 8 MV, it becomes progressively more significant, and may well become the predominant process, as the energy is increased beyond 10 MV. The information presented here should allow reasonable assessment of secondary electron spread up to 16 MV. Further information would be desirable for energies higher than those available to us.

From the standpoint of the radiotherapist selecting the optimum beam energy for a particular treatment, there may well be situations where the improvement in beam sharpness afforded by lower energy beams outweighs the improved penetration of higher energy radiation. Young & Kornelsen (1983) noted that because of the increased range of secondary electrons, further degradation of beam profiles took place in lower density materials and for this reason they favoured 4 MV rather than 10 MV X rays for treatments of head, neck and chest.

The lateral field irradiation of retinoblastoma tumours in children is a specific example where a sharp beam profile is essential. With this technique, the principle is to irradiate the tumour located at the rear of the eye whilst preserving the sensitive structures of the anterior chamber including the lens. Schipper (1983), Harnett et al (1987) and Glaeser & Quast (1987) have all reported geometrically similar techniques based on an additional collimating arrangement located closer to the patient then the standard collimator, in order to reduce the geometric penumbra. Field location was achieved by a contact lens arrangement located on the patient's eye and magnetically attached to the additional collimator. Although beam energy is not the sole criterion when choosing equipment on which to implement this technique, it is interesting that as far as the achievement of a sharp penumbra is concerned, noticeably better results were achieved at 6 MV than at 15 MV. The information presented in this paper generally supports this observation.

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References

Adams, D. G., 1964. The use of a 70 MeV synchrotron in cancer therapy. *Radiology, 83,* 785–806.

Bagne, F., 1980. A method for calculating megavoltage X-ray dose and dose parameters. *Medical Physics, 7,* 664–671.

Bjarngard, B. E. & Cunningham, J. R., 1986. Comments on "Validity of the concept of separating primary and scatter dose". *Medical Physics, 13,* 760–761.

Boyer, A. L. & Mok, E. C., 1986. Calculation of photon dose distributions in an inhomogenous medium using convolutions. *Medical Physics, 13,* 503–509.

Chui, C.-S. & Mohan, R., 1988. Extraction of pencil beam kernels by the deconvolution method. *Medical Physics, 15,* 138–144.

Cunningham, J. R., 1972. Scatter–air ratios. *Physics in Medicine and Biology, 17,* 42–51.

Cunningham, J. R., Shrivastava, P. N. & Wilkinson, J. M., 1972. Program IRREG—calculation of dose from irregularly shaped radiation beams. *Computer Programs in Biomedicine, 2,* 192–199.

Dawson, D. J., Harper, J. M. & Akinradewo, A. C., 1984. Analysis of physical parameters associated with the measurement of high energy X-ray penumbra. *Medical Physics, 11,* 491–497.

Day, M. J. & Farmer, F. T., 1958. The 4 MeV linear accelerator at Newcastle upon Tyne. *British Journal of Radiology, 31,* 669–682

Day, M. J., 1976. Specification and additivity of unsharpness in diagnostic radiology. *Physics in Medicine and Biology, 21,* 399–405.

Doi, K. & Rossmann, K., 1975. Evaluation of focal spot distribution by RMS value and its effect on blood vessel imaging in angiography. *Proceedings of the Society of Photo-Optical Instrument Engineers, 47,* 207–213.

Dutreix, J., Dutreix, A. & Tubiana, M., 1965. Electronic equilibrium and transition stages. *Physics in Medicine and Biology, 10,* 177–190.

Ford, R. C. & Nelson, W. R., 1978. *The EGS code. Computer Programs for the Monte Carlo Simulation of Electromagnetic Cascade Showers, SLAC Report 210* (Stanford Linear Accelerator Centre, Stanford, USA).

Glaeser, L. & Quast, U., 1987. Dosimetry for high precision radiotherapy of the eye. *Proceedings of the First European Mevatron Users Conference* (Siemens, Erlangen), pp. 155–161.

Harnett, A. N., Hungerford, J. L., Lambert, G. D., Hirst, A., Darlison, R., Hart, B. L., Trodd, T. C. & Plowman, P. N., 1987. Improved external beam radiotherapy for the treatment of retinoblastoma. *British Journal of Radiology, 60,* 753–760.

Haywood, J. K., Bomford, C. K. & Hatton, J. A., 1979. A less empirical method of representing megavoltage beams for use in rapid radiotherapy dose calculations. *British Journal of Radiology, 52,* 709–718.

ICRU, 1976. *Report 24. Determination of absorbed dose in a patient irradiated by beams of X or Gamma rays in radiotherapy procedures* (International Commission on Radiation Units and Measurements, Washington, USA).

JONES, R. C., 1958. On the point and line spread functions of photographic images. *Journal of the Optical Society of America, 48,* 934–937.

KORNELSEN, R. O. & YOUNG, M. E. J., 1982. Changes in the dose-profile of a 10 MV X-ray beam within and beyond low density material. *Medical Physics, 9,* 114–116.

MACKIE, T. R., SCRIMGER, J. W. & BATTISTA, J. J., 1985a. A convolution method of calculating dose for 15 MV X-rays. *Medical Physics, 12,* 188–196.

MACKIE, T. R., EL-KHATIB, E., BATTISTA, J., SCRIMGER, J., VAN DYK, J. & CUNNINGHAM, J. R., 1985b. Lung dose corrections for 6 and 15 MV X-rays. *Medical Physics, 12,* 327–332.

MARCHAND, E. W., 1964. Deriviation of the point spread function from the line spread function. *Journal of the Optical Society of America, 54,* 915–919.

MARCHAND, E. W., 1965. From line to point spread function: the general case. *Journal of the Optical Society of America, 55,* 352–354.

MOHAN, R. & CHUI, C.-S., 1985. Validity of the concept of separating primary and scatter dose. *Medical Physics, 12,* 726–730.

PETTI, P. L., GOODMAN, M. S., GABRIEL, T. A. & MOHAN, R., 1983. Investigation of buildup dose from electron contamination of clinical photon beams. *Medical Physics, 10,* 18–24.

PETTI, P. L., RICE, R. K., MIJNHEER, B. J., CHIN, L. M. & BJARNGARD, B. E., 1987. A heterogeneity model for photon beams incorporating electron transport. *Medical Physics, 14,* 349–354.

ROESCH, W. C., 1958. Dose for nonelectronic equilibrium conditions. *Radiation Research, 9,* 399–410.

ROESCH, W. C., 1968. In *Radiation Dosimetry*. Ed. by F. H. Attix & W. C. Roesch (Academic Press, New York).

ROSSMANN, K., 1969. Point spread-function, line spread-function and modulation transfer function: tools for the study of imaging systems. *Radiology, 93,* 257–272.

SASANE, J. B. & IYER, P. S., 1981. Relevance of radiation penumbra in high-energy photon beam therapy. *Strahlentherapie, 157,* 658–661.

SCHIPPER, J., 1983. An accurate and simple method for radiation therapy of retinoblastoma. *Radiotherapy and Oncology, 1,* 31–41.

SHAPIRO, G., OVADIA, J. & LAUGHLIN, J. S., 1955. Dosimetry of localized beams. *Radiology, 64,* 227–233,

SUTCLIFFE, J. F., 1980. Radiation beam profiles from the Mobaltron MS80. *British Journal of Radiology, 53,* 150–151.

YOUNG, M. E. J. & KORNELSEN, R. O., 1983. Dose corrections for low-density tissue inhomogeneities and air channels for 10 MV X-rays. *Medical Physics, 10,* 450–455.

1990, *The British Journal of Radiology*, *63*, 286–289

Response of murine small intestine to combined treatment with fostriecin and X rays

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Abstract. This radiobiological investigation was based on the measurements of crypt cell survival in mouse small intestine when the animals were injected with a single dose of fostriecin or streptomycin, and subsequently irradiated to the whole body with graded doses of X rays. The experimental data obtained indicated that fostriecin decreased the isoeffect dose to murine intestine by a factor of 2.3, whereas streptomycin did not influence the radiation response. The biological effects of fostriecin on various tumour cell systems *in vitro* and *in vivo* are briefly reviewed. The possible basic mechanisms involved in the radiosensitizing action of fostriecin and the implications of these results in the radiation protection of normal tissues are discussed.

Introduction

Antibiotic substances, in addition to being cytostatic, may also enhance the effect of ionizing radiation on different biological systems. Actinomycin-D, for example, increased the radiosensitivity of murine intestine (Hagemann & Concannon, 1972) and also lung (Colman et al, 1982). A similar effect of bleomycin on oesophagus has been reported by Phillips et al (1975). Burholt et al (1975) observed that adriamycin combined with abdominal irradiation of mice did not alter the number of surviving crypts in the jejunum, but reduced the post-irradiation compensatory hyperplasia. Our own investigations on reverin (pyrrolidino-methyl-tetracycline) showed that the antibiotic increased the number of eye anomalies in 9-day-old rat embryos from 25.8% (irradiation only) to 55.8% (Fritz-Niggli et al, 1974). Thus many antibiotic agents have been tested for their ability to alter the radiation response of murine normal tissues. The newly discovered antibiotic fostriecin has not been tested for its activity in this connection as far as we are aware. The following report is therefore based on the response of intestine, a critical tissue involved when the abdominal or pelvic regions are irradiated, to combined treatment with fostriecin and X rays. The radiobiological activity of fostriecin (derived from *Streptomyces pulveraceus*, subspecies *fostreus*, see Stampwala et al, 1983) on mouse intestine was also compared with that of a standard streptomycin preparation, which is in general use in the clinical treatment of some diseases.

Materials and methods

Female NMRI mice (25–30 g) were randomly divided into the following groups: untreated control group, mice receiving a single injection of the drug, those irradiated with graded doses of X rays only and those with a single injection of drug before irradiation. At least five animals were used for each of the experimental treatments given in this study. Experiments with fostriecin and streptomycin were done separately, but under similar conditions except for the drug applied, and were repeated.

Fostriecin (supplied by the Pharmaceutical Research Division of Warner–Lambert/Parke–Davis, Michigan, USA) and the standard streptomycin (streptomycin sulphate, Sigma Chemical Company, Montana, USA) were freshly dissolved in sterile isotonic saline and administered by intraperitoneal injection to mice 30 min before irradiation. The single injection of fostriecin or streptomycin was given at a dose of 25 mg/kg.

Animals, restrained without anaesthesia in ventilated plexiglass phantoms, were irradiated to the whole body with single graded doses of 200 kVp X rays (with a half value layer of 0.93 mm copper and a dose-rate of 75 cGy/min).

The biological assay, used for the estimation and plotting of surviving crypt cells in treated or control mice, was based on the method described by Withers and Elkind (1970). Four days post-irradiation, the animals were sacrificed by cervical dislocation and a piece of jejunum was fixed for routine histological preparation. Transverse sections, 5 μm thick, were stained with hematoxylin and eosin. To get an optimum average score, five histological sections (cut at 5 mm distances) were prepared from each mouse. Finally, the number of crypts per jejunal circumference were counted in control and treated groups of mice. The untreated mice had the largest number of crypts per jejunal circumference and in the treated animals the number of crypts was reduced depending on the size of the radiation dose delivered. The calculation of surviving crypt cells from crypt counts (Withers & Elkind, 1970) was based on the assumptions made on the mode of cell survival, its distribution, and the crypt regenerating capacity. From the data obtained on the average number of surviving crypt cells per jejunal circumference, dose–effect curves were fitted by linear regression analysis and the dose for 20 surviving crypt cells per circumference was determined for comparative purposes.

Results

From our previous experience with this experimental model used (Rao & Fritz-Niggli, 1985, 1988), doses in

Table I. Average number of surviving crypts per jejunal circumference in mice exposed to graded doses of X rays only or with pre-irradiation application of fostriecin

Treatment		Average number of crypts	Standard error
Fostriecin	X rays (cGy)		
None	None	136.7	2.2
	900	105.9	3.6
	1000	60.6	2.1
	1100	38.9	1.7
	1200	9.2	1.0
	1300	10.2	1.3
	1400	1.8	0.4
Applied[a]	None	142.7	2.6
	100	135.4	2.2
	200	141.0	2.3
	300	107.7	2.5
	400	79.3	3.5
	500	44.4	3.7
	600	8.1	0.8
	700	2.2	0.7
	800	0.0	0.0
	900	0.0	0.0

[a] Always a single dose of 25 mg/kg.

Table II. Average number of surviving crypts per jejunal circumference in mice exposed to graded doses of X rays only or with pre-irradiation application of streptomycin

Treatment		Average number of crypts	Standard error
Streptomycin	X rays (cGy)		
None	None	144.6	1.5
	900	115.6	2.1
	1000	112.5	2.2
	1100	63.5	3.2
	1200	53.6	3.9
	1300	42.2	2.0
	1400	5.5	0.5
Applied[a]	None	144.7	2.3
	900	113.6	2.0
	1000	84.8	2.4
	1100	58.4	3.9
	1200	26.1	3.1
	1300	13.1	1.3
	1400	5.4	1.4

[a] Always a single dose of 25 mg/kg.

the range 9–14 Gy (six dose groups) were chosen for the present investigations. However, in a preliminary experiment where a single injection of fostriecin was given 30 min before irradiation, the mice exhibited severe gastrointestinal syndrome and were all moribund with about 17% dead on the 4th day after treatment. Histological sections revealed no surviving crypts at all in a majority of the mice, although a score between 1 and 3 was observed in a few instances. Therefore this particular group (fostriecin plus X rays) was exposed to a lower X-ray dose range: 1–9 Gy (nine dose groups). Fostriecin or streptomycin administered to non-irradiated mice did not alter the average number of crypts per jejunal circumference. The average numbers of crypts per jejunal circumference in mice irradiated with graded doses of X rays alone, and those with X-ray doses combined with pre-irradiation application of fostriecin or streptomycin, are given in Table I and II respectively. The dose–effect curves estimated from the data listed in the tables are shown in Figs 1 (fostriecin) and 2 (streptomycin), separately for the sake of clarity, where the average numbers of surviving crypt cells per jejunal circumference are plotted as a function of the radiation dose applied.

For the experimental series with streptomycin, the dose for 20 surviving crypt cells with X rays alone was 13.10 Gy and for the combined treatment 12.30 Gy. However, in the case of fostriecin series, the isoeffect dose of 11.40 for X rays alone was reduced to 5 Gy when the drug was administered before irradiation. This highly radiosensitizing effect of fostriecin explains the observations made in the preliminary experiment mentioned above. In the lower X-ray dose range (1–9 Gy) used in the combined treatment, fostriecin reduced the survival of crypts to zero for the 8 Gy and 9 Gy dose groups.

Discussion

Fostriecin has been studied intensively for its effect on a variety of murine and human cancer cells. It is a novel antibiotic that has no bactericidal effect but is antimycotic (Mamber et al, 1986), active against tumour cells *in vitro* and in some cases also *in vivo* but inactive against solid tumours (Leopold et al, 1984). Details on the chemical structure of fostriecin and its analogues, its biological activity in relation to alterations in the chemical composition, as well as the influence of mode or route of administration on the biological activity have been presented by Leopold et al (1984). According to them, fostriecin prolonged the life span of mice bearing L1210 leukemia cells but had little or no activity against mouse solid tumours (M5076 sarcoma, B16 melanoma and Ridgway osteogenic sarcoma) or against human tumour xenografts, because of a reduced folate transport deficiency caused by the drug.

Another detailed *in vitro* study on fostriecin with human tumour colony assay has been reported by Scheithauer et al (1986). Taking malignant tumour samples from patients to establish *in vitro* cultures, exposing the tumour cells to the drug for 1 h and using more than 50% decrease in the tumour colony forming units as the criterion of effect, the authors have reported an *in vitro* response of 33% in ovary, 42% in breast and 38% in lung cancers. All these experimental observations indicate the real possibility of fostriecin being used clinically as a drug in the chemotherapy of some types of cancers in the future. Under these circumstances, it is important to examine the reaction of dose-limiting normal tissues to fostriecin application. Results

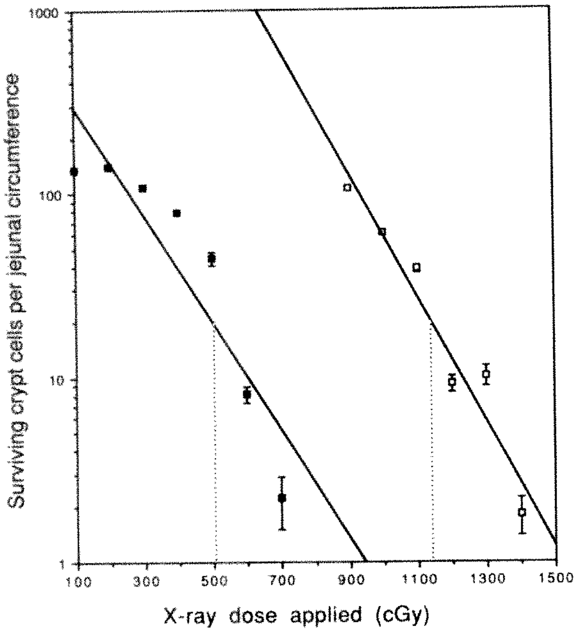

Figure 1. Dose–response curves for jejunal crypt cells in mice exposed to graded single doses of X rays only (□), or with pre-irradiation application of fostriecin (■). Ranges shown are within 95% confidence limits and the vertical dotted lines indicate the respective isoeffect dose for survival of 20 crypt cells per circumference.

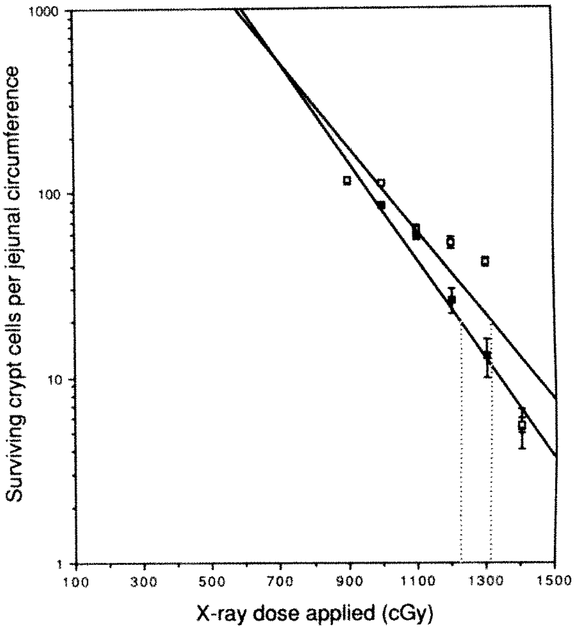

Figure 2. Dose–response curves for jejunal crypt cells in mice exposed to graded single doses of X rays only (□), or with pre-irradiation application of streptomycin (■).

presented here show that a single application of fostriecin at a 25 mg/kg dose had no effect on the number of jejunal crypts in mice. However, it should be noted that the effect of multiple injections of the drug on the intestine, a likely situation if the substance is employed in the chemotherapy of cancers, has not been investigated. This was partly because the main objective in this case was to examine the interaction of fostriecin and X rays on mouse intestine. Moreover, there is always a possibility of considering any new anticancer drug as a likely adjuvant treatment to routine radiotherapy.

Streptomycin, an antibiotic derived from a different species of *Streptomyces*, did not influence radiation response much, the ratio of isoeffect doses for X rays being 1.06. However, in the case of fostriecin, this ratio was 2.28, indicating that the drug more than doubled the damage to mouse intestine. It may be interesting to note that these antibiotic substances derived from two different species of the same genus, *Streptomyces*, show some differences in their biological activity. Streptomycin is bactericidal but fostriecin is not. The latter is active against tumour cells *in vitro* and partly *in vivo*, but the former is not. Fostriecin is a strong radiosensitizing agent, at least in this case, whereas streptomycin is not.

The basic mechanisms involved in the fostriecin-induced enhancement of mouse intestine radiosensitivity observed cannot be elucidated by this study. The cells investigated here have a strong inherent capacity to repair radiation damage (Rao & Fritz-Niggli, 1983). Thus any drug that interferes strongly with the repair mechanisms will severely enhance the radiosensitivity. Fry et al (1984) observed a decreased synthesis of DNA, RNA and protein in L1210 leukemia cells exposed to fostriecin. Such an inhibitory effect might result in a rapid accumulation of radiation-induced sublethal damage which would otherwise have been repaired. Thus the increased radiosensitivity due to fostriecin observed here may be due to the suppression of macromolecular synthesis and a consequent impairing of the repair system. The growth inhibitory action of fostriecin on human tumour cells *in vitro* was attributed by Scheithauer et al (1986) to a similar mode of action. As reported by Leopold et al (1984), fostriecin induced severe gastrointestinal toxicity in non-tumour-bearing mice treated with lethal (10–30% 7-day mortality) doses of the drug. Thus it may also be possible that the subsequent irradiation of fostriecin-treated mice drastically reduced the maximum tolerated dose level of the drug in the animals.

Whatever the basic mechanism involved in the radiosensitizing properties of fostriecin, our observations should be considered when a patient is treated with both fostriecin and X rays, for instance when fostriecin is given and X rays are applied for diagnostic purposes. The biological effect may be enhanced to a level far exceeding the normal tolerance for normal tissues.

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References

BURHOLT, D. R., HAGEMANN, R. F., COOPER, J. W., SCHENKEN, L. L. & LESHER, S., 1975. Damage and recovery assessment of the mouse jejunum to abdominal X-ray and adriamycin treatment. *British Journal of Radiology, 48,* 908–912.

COLMAN, M., ZABILANSKY, E. & REDPATH, J. L., 1982. Modification of the radiation response of mouse lung by actionomycin D: dependence on interval between radiation and drug treatments. *International Journal of Radiation Oncology, Biology, Physics, 8,* 511–512.

FRITZ-NIGGLI, H., MICHEL, C. & RAO, K. R., 1974. Sensitizing effect of reverin (pyrrolidinomethyltetracycline) on the radiation damage of rat embroys as compared to its effect on other cell systems. *Agents and Actions, 4,* 54–60.

FRY, D. W., BORITZKI, T. J. & JACKSON, R. C., 1984. Studies on the biochemical mechanism of the novel antitumor agent CI-920. *Cancer Chemotherapy and Pharmacology, 13,* 171–175.

HAGEMANN, R. F. & CONCANNON, J. P., 1972. Mechanisms of intestinal radiosensitization by actinomycin D. *British Journal of Radiology, 46,* 302–308.

LEOPOLD, W. R., SHILLIS, J. L., MERTUS, A. E., NELSON, J. M., ROBERTS, B. J. & JACKSON, R. C., 1984. Anticancer activity of the structurally novel antibiotic CI-920 and its analogues. *Cancer Research, 44,* 1928–1932.

MAMBER, S. W., OKASINSKI, W. G., PINTER, C. D. & TUNAC, J. B., 1986. Antimycotic effects of the novel antitumor agents fostriecin (CI-920), PD 113,270, and PD 113,271. *Journal of Antibiotics (Tokyo), 39,* 1467–1472.

PHILLIPS, T. L., WHARAM, M. D. & MARGOLIS, L. W., 1975. Modification of radiation injury to normal tissues by chemotherapeutic agents. *Cancer, 35,* 1678–1684.

RAO, K. R. & FRITZ-NIGGLI, H., 1983. Response of mouse small intestine to fractionated doses of pions. *Radiation and Environmental Biophysics, 21,* 247–254.

—— 1985. Effect of different pion stopping volumes on the radiation response of mouse small intestine. *International Journal of Radiation Biology, 48,* 61–69.

—— 1988. Alterations in the length of jejunal villi in mice irradiated with graded doses of X rays. *British Journal of Radiology, 61,* 839–842.

SCHEITHAUER, W., VON HOFF, D. D., CLARK, G. M., SHILLIS, J. L. & ELSLAGER, E. F., 1986. In vitro activity of the novel antitumor antibiotic fostriecin (CI-920) in a human tumor cloning assay. *European Journal of Cancer and Clinical Oncology, 22,* 921–926.

STAMPWALA, S. S., BUNGE, R. H., HURLEY, T. R., WILLMER, N. E., BRANKIEWICZ, A., STEINMAN, C. E., SMITKA, T. A., & FRENCH, J. C., 1983. Novel antitumor agents CI-920, PD 113,270 and PD 113,271. II. Isolation and characterization. *Journal of Antibiotics (Tokyo), 36,* 1601–1605.

WITHERS, H. R. & ELKIND, M. M., 1970. Microcolony survival assay for cells of mouse intestinal mucosa exposed to radiation *International Journal of Radiation Biology, 17,* 261–267.

1990, *The British Journal of Radiology*, *63*, 290–294

The use of small fraction numbers in high dose-rate gynaecological afterloading: some radiobiological considerations

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Abstract. Using commonly assumed α/β ratios for tumours and late-reacting tissues, the linear-quadratic (LQ) model has been used to compare low dose-rate (LDR) gynaecological treatment with high dose-rate (HDR) techniques given in small fraction numbers. Even in the absence of relatively favourable tissue recovery constants (μ values) it is shown that, provided a modest extra amount of geometrical sparing of critical tissues is available (by means of spacing or shielding), HDR treatment in a small number of fractions may be used in place of an LDR regime without loss of therapeutic ratio. This general result, although not universally true, does indicate that HDR treatment delivered in a small number of fractions may be more feasible than is sometimes thought. These findings do not contradict currently accepted radiobiological philosophy, which cautions against the use of small numbers of high-dose fractions. Primarily they serve to emphasize the importance of the recommendations of the ICRU (1985), which stress the need to consider the complete time–dose pattern of radiation delivery to all the critical tissues in an intracavitary treatment.

The radiobiological assessment of gynaecological brachytherapy treatments continues to be a subject of considerable interest. Although high dose-rate (HDR) afterloading units have been available for many years (*e.g.* O'Connell et al, 1967; Joslin et al, 1972), the growing availability of more sophisticated treatment machines has generated a concommitant requirement for a fuller understanding of the radiobiological pitfalls that might be associated with this form of treatment. Much remains to be properly understood, but the question of the optimal number of fractions to use is always of particular significance.

An in-depth appraisal of the possible link between low and high dose-rate treatments was undertaken by Liversage (1969). That analysis showed that, if a protracted low dose-rate (LDR) treatment lasting T hours is to be replaced by a HDR regime consisting of N fractions, the condition whereby the therapeutic ratio remains unchanged is that the same total dose is given in each case, with N being calculated from T by the relationship:

$$N = \frac{\mu T}{2\{1-[1-\exp(-\mu T)]/\mu T\}} \qquad (1)$$

where μ is the recovery constant, assumed to be the same for all the tissues. Liversage used a value for μ of 0.46 h^{-1} (corresponding to a recovery half-life of 1.5 h). For relatively large values of T this equation simplifies and, for the particular half-life chosen by Liversage, the derived relationship is better remembered as:

$$N \sim T/4 \qquad (2).$$

This general formula for equating N and T has been tested against experimental results for a variety of very different biological end points, at a variety of different dose-rates, and has been shown to be valid to within ±10% over the range of dose-rates tested (Liversage, 1969; Liversage & Dale, 1978; Turesson, 1978).

Although the original LDR regime will deliver different total doses to the various tissues (because of the dose-gradients), provided the LDR and HDR geometries are similar then the equivalence relationship between the two treatments remains true at all sites throughout the treatment volume.

The possible effects of tumour and acute normal-tissue proliferation are ignored in these formulae; for the equations to be strictly valid the N fractions would therefore need to be delivered in the same overall treatment time as the original LDR regime, *i.e.* in T hours. Although this would not be feasible in the majority of cases, it is clear from equations (1) and (2) that the theoretical number of HDR fractions would, in any case, usually be relatively large. For example, an LDR regime delivering 60 Gy in 72 h would need to be replaced by a fractionated regime that gives 60 Gy in approximately 18 (= 72/4) fractions.

In general, therefore, the satisfactory delivery of an HDR regime would appear to require a fraction number which is large enough to negate many of the logistic benefits of using such a treatment, and which is likely to be distressing for patients.

For fraction numbers less than that theoretically calculated from equation (2), Liversage (1969, 1987) predicted that a loss in therapeutic ratio (relative to the LDR regime) is to be expected, and the development of the linear-quadratic (LQ) formulation has enabled this aspect to be further quantified. It has been shown that the Liversage General Formula may be regarded as a special case of a more complex LQ relationship, the latter taking account of the tissue α/β ratios, in addition to their recovery constants (Dale, 1985, 1988). These aspects have been further discussed by Fowler (1989a).

Although the clinical value of using HDR gynaecological afterloading alone remains to be seen, many clinicians have found little difficulty in replacing, with fractionated HDR, the LDR intercavitary component of combined intracavitary/external beam treatments, and with significantly fewer intracavitary fractions than radiobiological calculations predict are necessary.

It is therefore appropriate to assess quantitatively the possible reasons for this. In this paper the nature of the inter-relationship between the geometrical sparing of the normal tissues and the fraction number will be examined in the light of the basic LQ formulation. The more complex case of intermediate dose-rate therapy is not addressed here.

Method

For fractionated HDR therapy, the standard LQ equation of Barendsen (1982), linking extrapolated response dose (ERD), relative effectiveness per unit dose (RE) and total dose (TD) is

$$\mathrm{ERD} = \mathrm{TD} \times \mathrm{RE} \qquad (3).$$

Using Barendsen's definition of RE we have

$$\mathrm{ERD} = Nd \times [1 + d/(\alpha/\beta)] \qquad (4)$$

where N fractions of magnitude d are used. Since the α/β ratio is characteristic of the tissue under consideration it follows that RE, and hence ERD, is also tissue specific. Therefore, even in a uniformly irradiated block comprising several different tissues, there will be separate ERD values that characterize the effects of the given dose on the individual tissues.

In general, late-reacting tissues are characterized by lower α/β ratios than are tumours (Fowler, 1989b). Equation (4) therefore shows why, for any given value of d, RE will usually be larger for late-reacting tissues than for tumours. Thus, reducing the dose/fraction has proportionately more effect on the late-reacting RE than on the tumour RE. This gives rise to the now well known argument that, where tumour and late-responding normal-tissue doses are the same, preferential sparing of the latter is more likely to be achieved with small doses/fraction.

In the case of a gynaecological application, there will almost certainly be large differences between the doses received by the tumour and the critical normal tissues, because of the large dose-gradients that exist. Although this is a seemingly obvious observation, there is still a common tendency to assess the efficacy of such treatments in terms of a nominal dose at an arbitrary reference point.

It is therefore important that radiobiological calculations are not made on the assumption that both the tumour and late-reacting tissues each receive the same total dose, and hence the same dose/fraction (or dose-rate). For the reasons outlined above, this assumption will invariably lead to the prediction that a relatively large number of HDR fractions will be required if a satisfactory therapeutic ratio is to be maintained.

If the dose to a late-reacting critical tissue (the rectum, say) is some known fraction (f) of the true tumour dose, then we may write separate ERD equations for both the HDR and LDR cases. In the HDR case,

(a) for the tumour:

$$\mathrm{ERD}_{\mathrm{tum}} = Nd \times [1 + d/(\alpha/\beta)_{\mathrm{tum}}] \qquad (5)$$

(b) for the late-reacting critical tissue:

$$\mathrm{ERD}_{\mathrm{late}} = fNd \times [1 + fd/(\alpha/\beta)_{\mathrm{late}}] \qquad (6)$$

where the suffixes indicate the effects referred to. It should be noted that the factor f appears twice in equation (6), since both the total dose and the dose/fraction are changed in the same proportion. Similarly, in the LDR case,

(c) for the tumour:

$$\mathrm{ERD}_{\mathrm{tum}} = RT \times [1 + 2R/\{\mu_{\mathrm{tum}}\,(\alpha/\beta)_{\mathrm{tum}}\}] \qquad (7)$$

(d) for the late-reacting critical tissue:

$$\mathrm{ERD}_{\mathrm{late}} = fRT \times [1 + 2fR/\{\mu_{\mathrm{late}}(\alpha/\beta)_{\mathrm{late}}\}] \qquad (8)$$

These are the ERD equations for LDR when the treatment time (T) is relatively long (Dale, 1985). R is the dose-rate, delivered over time T. For intermediate dose rates (and hence intermediate treatment times), equations (7) and (8) are no longer valid.

Clinical example

Although generalized solutions to the above equations are possible, it is useful to examine initially one particular case. Suppose that an LDR treatment of the cervix delivers 60 Gy in 72 h to the tumour (*i.e.* at a dose-rate of 0.833 Gy h^{-1}) and that, because of geometrical sparing (*i.e.* the combination of shielding and physical spacing), the rectum receives 80% of this dose, *i.e.* the time–dose pattern for this organ is 48 Gy in 72 h, at a dose-rate of 0.667 Gy h^{-1}. Assuming respective late-reacting and tumour α/β ratios of 3 Gy and 10 Gy (Fowler, 1989b), we can calculate the ERDs associated with the original treatment using equations (7) and (8):

$$\mathrm{ERD}_{\mathrm{tum}} = 60 \times [1 + (2 \times 0.833)(0.46 \times 10)] = 81.7\ \mathrm{Gy}.$$

$$\mathrm{ERD}_{\mathrm{late}} = 0.8 \times 60 \times [1 + (2 \times 0.8 \times 0.833)(0.46 \times 3)] = 94.4\ \mathrm{Gy}.$$

Now let us assume that the LDR treatment is to be replaced by a HDR afterloading regime delivered in six fractions and that, because of identical geometry in the two techniques, the rectal dose may be restricted to 80% of the tumour dose, as before. To maintain the tumour effect we must first find the combination of total dose and dose/fraction which gives the same tumour ERD of 81.7 Gy, *i.e.* use equation (5) and solve

$$81.7 = 6d \times (1 + d/10)$$

where d is the tumour dose/fraction.

This equation may be solved as a quadratic equation, and leads to a d value of 7.7 Gy, *i.e.* the total dose at HDR required to maintain the tumour effect is $6 \times 7.7 = 46.2$ Gy. Substituting this value of d back into

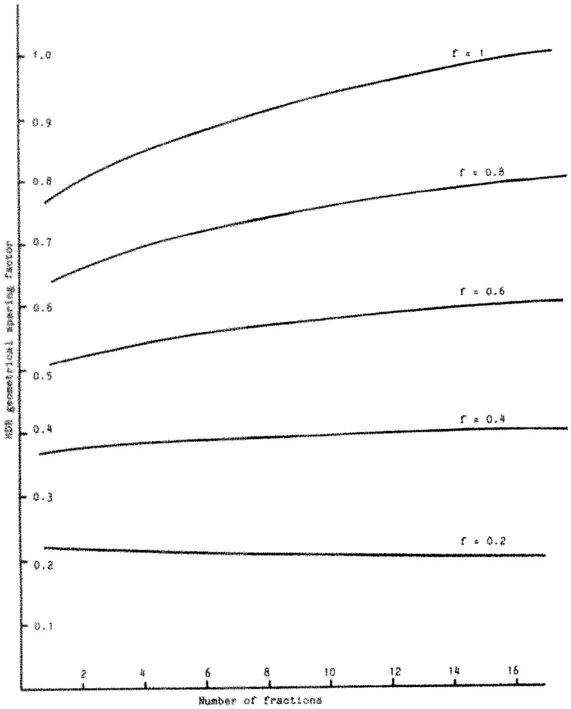

Figure 1. The HDR geometrical sparing factor which is necessary to maintain the biological effect on late-reacting tissues for various values of LDR geometrical sparing factor (f) is demonstrated. The reference LDR regime is assumed to deliver 60 Gy in 72 h to the tumour, and all of the HDR regimes have been calculated to produce the same tumour effect (*i.e.* the same tumour ERD). The sparing factor is the dose to the critical (late-reacting) tissue divided by the tumour dose, and is achieved by a combination of spacing and shielding. (Assumed α/β ratios: 3 Gy for late-reactions; 10 Gy for tumours. Assumed μ values: 0.46 h^{-1} for both tissues.)

equation (6) for the late-reacting tissue, again using $f = 0.8$, we find

$$\mathrm{ERD}_{\mathrm{late}} = 0.8 \times 6 \times 7.7 \times [1 + (0.8 \times 7.7/3)] = 112.9\ \mathrm{Gy}.$$

This value of the late-reacting ERD is around 20% higher than that associated with the original LDR treatment (94.4 Gy), and therefore the six fraction HDR treatment has produced a marked deterioration in therapeutic ratio, in accordance with standard radiobiological predictions.

The pertinent question to ask next is this: how much additional geometrical sparing of the critical tissue (in this case the rectum) is required in order to ensure that the original late-reacting ERD value is not exceeded, *i.e.* to ensure that therapeutic ratio is not lost in the switch from LDR to HDR?

This calculation is easily performed, again using equation (6). In this case we must find a new value for the sparing factor (f) which enables the above criterion to be met, *i.e.* we must solve, for f, the following:

$$94.4 = 6 \times f \times 7.7 \times [1 + (f \times 7.7)/3].$$

Again this may be solved as a quadratic equation, and yields $f = 0.72$, *i.e.* in the six fraction HDR case there need be no deterioration in therapeutic ratio (relative to the LDR case) if the rectal dose is restricted to 72% (or less) of the tumour dose. As the assumed geometrical sparing factor in the original LDR case was 0.8 (*i.e.* the rectum received 80% of the tumour dose), the additional geometrical sparing necessary to negate the expected 20% loss in therapeutic ratio, and which makes the HDR treatment a more attractive alternative, is very modest and is probably more easily obtainable (at least for the rectum) with reproducible source restraint during short HDR treatments.

That such an improvement may be brought about by a relatively small geometrical change is easily explainable in terms of basic LQ postulations. The key feature of the formulation is that the effectiveness of a dose of radiation may be assessed in numerical terms that take account of the manner (in terms of dose-rate or dose/fraction) in which that dose is delivered. Therefore the model demonstrates, more clearly than previous radiobiological systems, that a statement of the total doses received by various critical tissues is, by itself, a very poor indicator of the likely biological effects.

Changing the geometrical sparing factor affects both the total dose and the dose/fraction, and the overall radiobiological sparing is not therefore linearly related to the change in dose; in fact it varies more rapidly. These features of the LQ model are well understood and widely quoted in applications of the formulation to external beam radiotherapy, and their application to the intercomparison of HDR and LDR gynaecological treatments goes some way to indicating why the use of HDR treatments with relatively small fraction numbers may be a clinically viable proposition.

Discussion

For the same initial LDR regime assumed above (60 Gy in 72 h), and for various other LDR geometrical sparing factors, the above sequence of calculations has been repeated for a range of fraction numbers. The results, again assuming a dose recovery constant of 0.46 h^{-1} for both tumour and late-reacting tissue, are summarized graphically in Fig. 1.

The following features are noteworthy:

(a) When there is a good degree of geometrical sparing in the original LDR regime, very little further improvement is required in the corresponding HDR regime to enable therapeutic ratio to be maintained with small fraction numbers.

(b) When there is no LDR geometrical dose sparing of the critical tissue (*i.e.* $f = 1$), only a modest improvement is required (around 10–15%) to enable small fraction HDR treatments to be used without loss of therapeutic ratio.

(c) When the number of HDR fractions is that calculated by the Liversage General Formula (given by equation (1); in this case $(0.46 \times 72)/2 = 16.6$) the geometrical sparing factor at HDR need only be the same as that in the LDR case.

Although other considerations, such as tumour repopulation effects, have been ignored here, their inclusion would not have a large influence on the general findings. Also it will be found that these conclusions are qualitatively true irrespective of the "target" tumour ERD used as a starting point for the calculations.

It would further appear from Fig. 1 that even single fraction treatments are feasible, provided there is adequate geometrical spacing or shielding, but considerable caution must be exercised in this, for two reasons.

First, the LQ model may begin to break down when dose/fraction is large, and the predictive reliability of the model is therefore more suspect for very small fraction numbers (Gilbert et al, 1980; Thames, 1985; Dale, 1987; Orton, 1987). Secondly, because of the acknowledged importance of fraction size, treatments given in very small fraction numbers are likely to be less "forgiving" of dosimetry changes resulting from relatively small variations in geometry. This may be particularly relevant when, as in the case of HDR cervix treatments, more than one critical tissue is involved.

In cases where the tumour recovery constant is greater than that for late-reacting tissues, it has already been demonstrated (Orton, 1987) that HDR afterloading with small fraction numbers is favourable and that, even if tumour and normal tissues receive the same time-dose pattern of irradiation (*i.e.* there is no geometrical sparing), maintenance of, or improvement in, therapeutic ratio is fairly easily achieved.

However, as has been pointed out by Dale (1987), it is unwise to make generalizations about tumour μ values, and recent studies on human carcinoma of the cervix lines (Kelland & Steel, 1988) have indicated that wide variations in this parameter indeed exist. Caution must therefore be exercised in interpreting radiobiological intercomparisons that use only favourable parameters. If tumour recovery half-lives are significantly longer than 1.5 h, as they may be in some cases, then it may be that insufficient extra HDR geometrical sparing would be available to maintain the original therapeutic ratio.

A further caution is that the assumed repair mechanism in the LQ calculations used here is mono-exponential in form. The work of Hopewell and van den Aardweg (1988), amongst others, has indicated that there may exist other types of repair mechanism of a biphasic nature, although there has so far been no statistically unambiguous demonstration that such effects exist (Thames et al, 1989).

Although there is truth in the statement that most measured tumour α/β values have been found to be higher than those for late-reacting normal tissues, there are known exceptions to the general rule. Where the late-normal tissue α/β ratio is greater than the tumour α/β ratio there is automatically a more favourable case for small fraction numbers, since hypo-fractionation can be expected to improve therapeutic ratio in such cases.

There can be little doubt that LDR continuous radiotherapy represents a good form of treatment, for a number of sound radiobiological reasons (Dale, 1989; Fowler, 1989a; Steel et al, 1989). The point emerging from this article is that small-fraction HDR therapy may in some circumstances also be used with some success, even if the respective values of tumour and late-reacting recovery constants do not appear immediately favourable to the technique. Indeed, the careful use of fixed-geometry HDR techniques provides an opportunity to attempt to reduce further the dose to some, if not all, critical structures.

It is a key recommendation of ICRU Report 38 (ICRU, 1985) that, in the reporting of a brachytherapy treatment, a complete description of the doses and the dose–time patterns of radiation delivery to all relevant sites, rather than merely total dose, is necessary. In this presentation it has been possible to demonstrate the clinical relevance of such considerations in relation to HDR afterloading with small fraction numbers, the use of which allows the realization of a number of logistic and economic advantages.

Acknowledgments

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References

Barendsen, G. W., 1982. Dose fractionation, dose-rate, and iso-effect relationships for normal tissue response. *International Journal of Radiation Oncology, Biology, Physics*, *8*, 1981–1997.

Dale, R. G., 1985. The application of the linear-quadratic dose-effect equation to fractionated and protracted radiotherapy. *British Journal of Radiology*, *58*, 515–528.

—— 1987. What minimum number of fractions is required with high dose-rate remote afterloading? (Reply to letter by C. G. Orton.) *British Journal of Radiology*, *60*, 300–302.

—— 1988. Radiobiology of changes in dose-rate. In *High Dose-rate Afterloading in the Treatment of Cancer of the Uterus, Breast and Rectum*. Ed. by H. Vahrson & G. Rauthe (Urban and Schwarzenberg, Munich), pp. 24–29.

—— 1989. Time-dependent tumour repopulation factors in linear-quadratic equations—implications for treatment strategies. *Radiotherapy and Oncology*, *15*, 371–382.

Fowler, J. F., 1989a. Dose-rate effects in normal tissues. In *Brachytherapy 2: Proceedings of the 5th International Brachytherapy Working Conference*. Ed. by R. F. Mould (Nucletron International B.V., Leersum, The Netherlands), pp. 26–40.

—— 1989b. The linear-quadratic formula and progress in fractionated radiotherapy (Review article). *British Journal of Radiology*, *62*, 679–694.

Gilbert, C. W., Hendry, J. H. & Manor, D., 1980. The approximation in the formulation for survival $S = \exp-(\alpha D + \beta D^2)$. *International Journal of Radiation Biology*, *37*, 469–471.

Hopewell, J. W. & van den Aardweg, G. J. M. J., 1988. Current concepts of dose fractionation in radiotherapy. Normal tissue tolerance. In *Megavoltage Radiotherapy, 1937–1987. British Journal of Radiology Suppl. 22*. Ed. by P. N. Plowman & A. N. Harnett (British Institute of Radiology, London), pp. 88–94.

ICRU, 1985. *Dose Volume Specification for Reporting Intracavitary Therapy in Gynaecology. Report 38* (International

Commission on Radiation Units and Measurements, Bethesda, Maryland, USA).

JOSLIN, C. A. F., SMITH, C. W. & MALIK, A., 1972. The treatment of cervix cancer using high-activity cobalt 60 sources. *British Journal of Radiology, 45*, 257–270.

KELLAND, L. R. & STEEL, G. G., 1988. Differences in radiation response among human cervix carcinoma cell lines. *Radiotherapy and Oncology, 13*, 225–232.

LIVERSAGE, W. E., 1969. A General Formula for equating protracted and acute regimes of radiation. *British Journal of Radiology, 42*, 432–440.

LIVERSAGE, W. E., 1987. Radiobiological aspects. In *Radionuclides in Brachytherapy: Radium and After. British Journal of Radiology, Suppl. 21.* Ed. by N. G. Trott (British Institute of Radiology, London), pp. 34–40.

LIVERSAGE, W. E. & DALE, R. G., 1978. Dose–time relationships in irradiated weevils and their relevance to mammalian systems. *Current Topics in Radiation Research Quarterly, 13*, 97–187.

O'CONNELL, D., JOSLIN, C. A., HOWARD, N., RAMSEY, N. W. & LIVERSAGE, W. E., 1967. Treatment of uterine carcinoma using the cathetron. *British Journal of Radiology, 40*, 882–887.

ORTON, C. G., 1987. What minimum number of fractions is required with high dose-rate afterloading? (Letter). *British Journal of Radiology, 60*, 300–302.

STEEL, G. G., KELLAND, L. R. & PEACOCK, J. H., (1989). The radiobiological basis for low dose-rate radiotherapy. In *Brachytherapy 2; Proceedings of the 5th International Brachytherapy Working Conference*. Ed. by R. F. Mould (Nucletron International B.V., Leersum, The Netherlands), pp. 15–25.

THAMES, H. D., 1985. An "incomplete-repair" model for survival after fractionated and continuous irradiations. *International Journal of Radiation Biology, 47*, 319–339.

THAMES, H. D., MASON, K. A., BENTZEN, S. M., KIAN ANG, K. & CUNDIFF, J. H., 1989. Split-dose recovery in mouse jejunal crypt cells: characterisation of repair kinetics. In *The Scientific Basis of Radiotherapy. British Institute of Radiology Report 19.* Ed. by N. J. McNally (British Journal of Radiology, London), pp. 37–42.

TURESSON, I., 1978. Fractionation and dose-rate in radiotherapy. An experimental and clinical study of cumulative radiation effects. *MD Thesis.* University of Goteborg, Sweden.

1990, *The British Journal of Radiology*, *63*, 295–298

Technical notes

Peripheral doses of two linear accelerators employing universal wedges

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The peripheral dose (PD) is defined as the dose delivered to tissues outside the collimated radiotherapy beam. This absorbed dose will be of clinical concern if any uninvolved radiosensitive or critical structures outside the beam were to receive dosages approaching their tolerance levels. Sources of the PD include head leakage (transmission through the collimation system), collimator scatter, scatter and secondary particle production from a beam modifier (tissue compensator, wedge filter or shielding) present in the beam and scatter arising from within tissue. A fifth source, that due to radioactivity induced within the patient by a high-energy beam, is not considered in this work.

In the past, several studies have been undertaken to characterize the peripheral dose as a function of beam modality and quality, field dimension, the separation between the radiation source and the patient and the presence and composition of a beam modifier (Keller et al, 1974; Scrimger & Kolitsi, 1979; Nusslin & Hassenstein, 1980; Fraass & van de Geijn, 1983; Greene et al, 1983; Kase et al, 1983; Starkschall et al, 1983; Greene et al, 1985; Sherazi & Kase, 1985; Francois et al, 1988). Peripheral doses at specific clinical sites, such as the contralateral breast (Fraass et al, 1985) and the gonads (Yau et al, 1981), have also been measured on patients and within anthropomorphic phantoms. In general, these studies indicate that the PD decreases approximately exponentially with distance from the beam edge. Kase et al (1983) measured the various components of the PD for a number of photon beam qualities and showed that collimator scatter can comprise up to 40% of the total peripheral dose. Greene et al (1985), however, determined that collimator scatter is the dominant component of the peripheral dose for the X rays from two linear accelerators identical to the ones discussed in this paper. These two analyses suggest that collimator design and structures within the treatment head can have a strong effect upon the PD.

The introduction of a beam modifier, such as a wedge filter, will increase the peripheral dose as a result of scatter of the incident beam and the generation of secondary electrons incident to tissue. In addition, because of the beam attenuation by the modifier, a higher number of monitor units is required in order to deliver the same dose as for an open field. Consequently, the collimator scatter and head leakage components of the PD for a wedged field are expected to be elevated. Scrimger and Kolitsi (1979) showed that the peripheral dose for ^{60}Co photons and 8 MV X rays is elevated by the presence of a modifier and that the PD decreased with an increase in the modifier–surface distance. Sherazi and Kase (1985) measured the effects of wedge filters on the PD and showed that a conventional wedge filter can elevate the PD by factors of 2–4 over that for the open field, depending on the wedge angle. Additionally, they showed that whereas near the beam, in-phantom and wedge scatter contribute equally to the total peripheral dose, the wedge scatter component dominates at distances beyond about 15 cm from the field edge. Fraass et al (1985) determined that a wedge filter used as a tissue compensator within the medial tangential field for primary breast irradiation can increase the contralateral breast dose per unit given dose to the target breast over that of an unwedged field by factors approaching 5.

Some new linear accelerators employ an internal universal wedge filter, which is a single steep wedge filter mounted within the treatment head, at an extended distance from the patient. The wedge filter is inserted into the beam by a motor drive. Suitable admixtures of wedged and open (unwedged) fields allow the generation of any effective wedge angle up to that of the universal wedge (Petti & Siddon, 1985). As such a wedge is placed at a considerable distance from the patient, and because any scattered radiations from the wedge will be heavily filtered by structures within the treatment head, the results of Scrimger and Kolitsi (1979) and Sherazi and Kase (1985) suggest that the peripheral dose of an accelerator with a universal wedge filter may be less than that of an accelerator using a wedge filter placed in the more customary position between the treatment head and the patient.

This paper describes a series of basic measurements performed to characterize the effects of a universal wedge upon the peripheral dose. Peripheral dose profiles were obtained for open and wedged fields for two linear

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accelerators using universal wedges and generating 6 MV and 10 MV X rays. The PD is presented as a percentage of the central axis maximum and as a function of field dimension, wedge orientation and distance from the geometric field edge.

Materials and methods

Two linear accelerators (Philips/MEL SL75/5 and SL75/14N) producing 6 MV and 10 MV X rays, respectively, were studied. Each machine is equipped with an internal universal 60° wedge mounted within the treatment head between the transmission monitor chamber and the variable collimators, at a distance of 81 cm above the isocentre. Because of the machine designs, the wedged field dimension is restricted to 20 cm or less along the wedge plane.

Ionization measurements were performed in a 50 × 50 × 48 cm water phantom (Nuclear Associates Beamscan) for a vertically incident beam using a Physikalisch-Technische Werkstatten (PTW) 0.1 cm^3 ionization chamber, mounted normal to the beam axis, and a PTW IQ4 electrometer. The position of the ionization chamber was controlled by a PTW MP2 electronic drive mechanism with a spatial resolution of 0.1 mm. The electrometer and drive controller were interfaced to a Hewlett–Packard 9122 microcomputer and the integrated charge and chamber spatial position were stored on disk for later analysis. The absorbed dose rates at the central axis maxima were approximately 7 cGy/s and 10 cGy/s for the 6 MV and 10 MV beams, respectively.

Ionization profiles were measured at a 100 cm source–skin distance from 1 cm beyond the geometric field edge at the depth considered up to a maximum distance of 30 cm in increments of either 2 mm or 5 mm. Profiles were measured only along the wedge plane for open fields and for wedged fields with the wedge filter oriented with either the thick end ("heel") or thin end ("toe") towards the measurement direction. The wedge orientation was changed by rotating the treatment head by 180°. Any collimator asymmetry or misalignment between the accelerator beam axis and the phantom central axis was checked by comparing the open field profiles for the two different head rotations differing by 180°; any disagreement between the two profiles was less than the statistical uncertainty discussed below.

The measured reproducibility of the raw ionization data was better than $\pm 1.5\%$ about the mean (1 standard deviation). As all the results presented here are normalized to the maximum central axis ionization, the results provided have a maximum statistical uncertainty of $\pm 2.5\%$ about the mean. Temporal variations in accelerator output or the detector electronics were constantly tested and corrected for by regularly measuring the absolute dose output per unit time at the central axis maximum and the central axis depth dose before and after each peripheral dose measurement.

Results and discussion

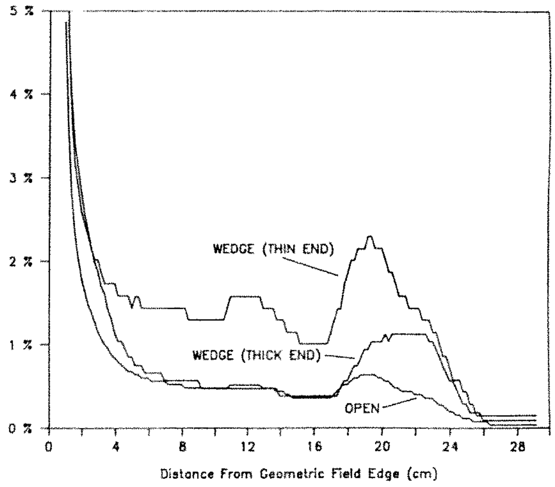

Figure 1. Peripheral dose profile for the 10 MV X-ray beam at a depth of 2.5 cm for the 5 × 5 cm field.

Profiles were measured in water for 5 × 5, 10 × 10 and 15 × 15 cm fields for both machines at the depth of the maximum central axis dose (1.5 cm and 2.5 cm for 6 MV and 10 MV X rays, respectively) and at depths of 5 and 10 cm. The data presented here are given as percentages of the measured central axis maximum ionization for the field and wedge condition considered and as functions of the distance from the geometric field edge at depth. The conversion from percentage ionization to percentage absorbed dose requires detailed knowledge of the photon energy spectrum, which was unavailable for the points outside the beam that were considered here. As the ratio of mass energy absorption coefficients for water to air exhibits a limited energy dependence for megavoltage photons, the percentage ionization data discussed in this work will be representative of the percentage absorbed dose.

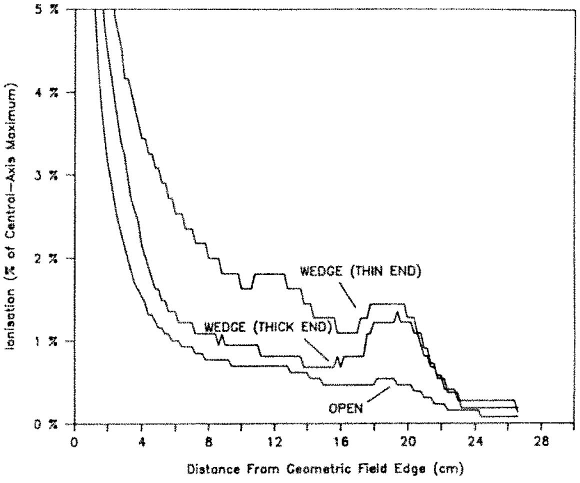

Figure 2. Peripheral dose profile for the 10 MV X-ray beam at a depth of 2.5 cm for the 10 × 10 cm field.

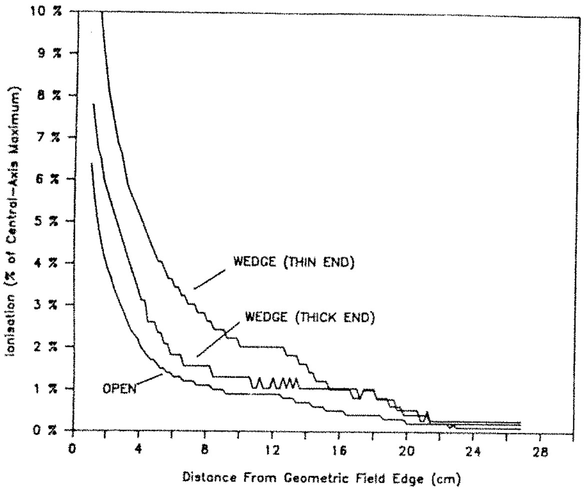

Figure 3. Peripheral dose profile for the 10 MV X-ray beam at a depth of 2.5 cm for the 15 × 15 cm field. Note the change in scale from Figs 1 and 2.

Figures 1, 2 and 3 show profiles measured in 2 mm increments for 10 MV X rays at a depth of 2.5 cm for open and wedged fields and for all three field dimensions for distances up to 30 cm from the geometric field edge. As very similar profiles were exhibited by the 6 MV X rays, only the 10 MV data are presented here. The peripheral dose measured here showed a very limited depth dependence, as also noted by Fraass and van de Geijn (1983) and Kase et al (1983), varying by less than 1% of the central dose maximum for depths between $d_{\max}$ and 10 cm.

All the profiles exhibit an approximate exponential decrease with off-beam distance. Peaks are observed in the 5 × 5 and 10 × 10 cm profiles at about 20 cm from the geometric field edge, as noted previously by Greene et al (1983, 1985), and are attributed to photons scattered from the opposite proximal variable collimator face. The magnitudes of these peaks decrease with increasing field dimension and the lateral separation between the peaks and the field edge show a dependence upon wedge orientation. A much smaller elevation in ionization is visible at 12 cm from the beam edge for the 5 × 5 cm profile and, to a much lesser degree, for the 10 × 10 cm profile measured proximal to the thin end of the wedge. These peaks do not appear in the data of Greene et al (1983, 1985), probably because of their coarser measurement increment relative to that used here.

The increase in the PD owing to the universal wedge is strongly dependent on the wedge orientation and, to a lesser degree, on field dimension. The PD proximal to the thick end of the wedge does not show a significant increase for the wedged field for the 5 × 5 cm and 10 × 10 cm dimension (except at the peak), but increases slightly by a factor of about 1.3 for the 15 × 15 cm field. In contrast, the PD proximal to the thin end of the wedge is markedly increased by factors of 2–3. This dependence of the PD magnitude on the wedge orientation is presumably a result of the variation in attenuation across the wedge with resulting variations in collimator and in-phantom scatter. Additional measurements using the methods described by Sherazi and Kase (1985) would be of interest in determining the magnitudes of the PD components for a universally wedged field.

Conclusions

For certain clinical sites, the peripheral dose generated by a radiotherapy beam may be of some concern. It has been noted in the literature that scatter from a beam modifier such as a wedge filter can increase the peripheral dose over that received from an open field for the same given dose. The effect of the beam modifier on the peripheral dose has also been reported to increase with its proximity to the surface. As a result, an internal universal filter, being at an extended distance from the patient and shielded by structures within the treatment head, may be expected to generate a reduced peripheral dose relative to that for an accelerator with a wedge mounted proximal to the patient.

This paper has discussed detailed peripheral dose measurements made on two linear accelerators, each equipped with an internal 60° universal wedge filter. The peripheral dose, normalized to the maximum central axis dose, is elevated by the presence of a universal wedge filter. It was found that, for the same maximum central axis dose, the universial wedge can readily elevate the PD by factors of 2–3 over that of the open field, depending upon the wedge orientation and field dimension. These factors tend to be less than those reported previously in the literature for a wedge filter mounted in the more conventional fashion. In practice, because effective wedge angles are formed by combinations of wedged and unwedged fields, the net increase in the PD would generally be less than that measured here for the fully wedged field.

The clinical impact of this result is currently being studied with an anthropomorphic phantom and *in situ* thermoluminescence dosimetry (TLD) measurements of patients, treated with fields employing the universal wedge, at sites such as the contralateral breast or the cornea.

References

Fraass, B. A. & van de Geijn, J., 1983. Peripheral dose from megavolt beams. *Medical Physics, 10,* 809–818.

Fraass, B. A., Roberson, P. L. & Lichter, A. S., 1985. Dose to the contralateral breast due to primary breast irradiation. *International Journal of Radiation Oncology, Biology, Physics, 11,* 485–497.

Francois, P., Beurtheret, C. & Dutreix, A., 1988. Calculation of the dose delivered to organs outside the radiation beams. *Medical Physics, 15,* 879–883.

Greene, D., Chu, G.-L. & Thomas, D. W., 1983. Dose levels outside radiotherapy beams. *British Journal of Radiology, 56,* 543–550.

Greene, D., Karup, P. G. G., Sims, C. & Taylor, R. J., 1985. Dose levels outside radiotherapy beams. *British Journal of Radiology, 58,* 453–456.

Kase, K. R., Svensson, G. K., Wolbart, A. B. & Marks, M.

1990, *The British Journal of Radiology*, *63*, 298–301

A., 1983. Measurements of dose from secondary radiation outside a treatment field. *International Journal of Radiation Oncology, Biology, Physics*, *9*, 1177–1183.

Keller, B., Mathewson, C. & Rubin, P., 1974. Scattered radiation dose as a function of X ray energy. *Radiology*, *111*, 447–449.

Nusslin, F. & Hassenstein, E., 1980. Measurements on the radiation protection of patients irradiated with an 18-MeV electron linear accelerator. *Strahlentherapie*, *156*, 120–124.

Petti, P. & Siddon, R. L., 1985. Effective wedge angles with a universal wedge. *Physics in Medicine and Biology*, *30*, 985–991.

Scrimger, J. & Kolitsi, Z., 1979. Scattered radiation from beam modifiers used with megavoltage units. *Radiology*, *130*, 233–236.

Sherazi, S. & Kase, K. R., 1985. Measurements of dose from secondary radiation outside a treatment field: effects of wedges and blocks. *International Journal of Radiation Oncology, Biology and Physics*, *11*, 2171–2176.

Starkschall, G., St George, F. J. & Zellmer, D. L., 1983. Surface dose for megavoltage photon beams outside the treatment field. *Medical Physics*, *10*, 906–910.

Yau, Y.-A., Huang, S.-H., Hsu, P.-C. & Weng, P.-S., 1981. Gonadal dose obtained from treatment of nasal carcinoma by ionizing radiation. *Radiation Research*, *86*, 147–151.

Neutron and gamma ray measurements carried out around a Varian Clinac 2500 linear accelerator*

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Auckland Hospital, New Zealand, has recently installed a Varian Clinac 2500 linear accelerator. This unit is capable of producing 24 MV peak photon energies. It is well known (Fox et al, 1977; Ing et al, 1982; Palta et al, 1984) that such photons are capable of producing neutrons via a photonuclear reaction. The sources of such neutrons from this accelerator have been described (LaRiviere, 1985). In this study a survey was carried out around this new installation to observe some of the characteristics of the neutrons produced, and to assess likely radiological hazards to radiotherapy staff.

Equipment and methods

Equivalent neutron dose was measured using an Alnor neutron dose rate meter (rem-meter) model 2202D. Remote pulse counting was carried out using an Elscint model INS-30 nuclear spectrometer.

The manufacturer of this unit claims that the detector exhibits 200 R/h gamma ray discrimination. Initially this would appear satisfactory for carrying out a survey, but owing to the fact that linear accelerators are operated in pulsed mode, peak leakage and scatter photon dose rates within the treatment room could well exceed 200 R/h. This was confirmed by operating the accelerator in 6 MV photon mode (*i.e.* producing no expected neutrons) and showing that the neutron meter did in fact respond. However, in the entrance maze to the treatment room the scattered X-ray dose rate was attenuated sufficiently so that it was not contributing to detector response.

X-ray leakage measurements were carried out using a Philips XL 1000/10 gamma survey meter, which is a large volume ionization chamber. A thermal neutron detection system was also used for comparison purposes with the Alnor rem-meter. This system is described in another paper (Beckham & Entwistle, 1987), but is based on a ^{6}Li glass scintillation crystal (NE912) and photomultiplier tube combination.

Therapy radiographers were considered to be most likely to receive the greatest radiation dose at the facility owing to the nature of their work, requiring them to be present at all times in the immediate environs of the treatment room. The following sources of exposure were quantified: leakage photons (including prompt capture gamma rays), exposure from radioactive neutron activation products and leakage neutrons.

Results

Calculation of maximum expected therapy radiographer dose

The position of the dose assessment for the case of leakage photons and neutrons was position 10 in Fig. 1. This was the site with the highest detectable dose rates outside of the treatment room. "Typical" machine parameters were used, namely 300 cGy/min isocentre X-ray dose rate and primary jaw settings of $20 \times 20\,\mathrm{cm}^2$. A "worst case" weekly workload with the 24 MV beam was assumed of 72 000 cGy/week to enable calculation of maximum equivalent dose rates. In practice the bulk of the work of the Auckland machine will be with 6 MV photons and the six electron modes.

Leakage photon dose rate. With the machine operating in the 24 MV photon mode the dose rate due to

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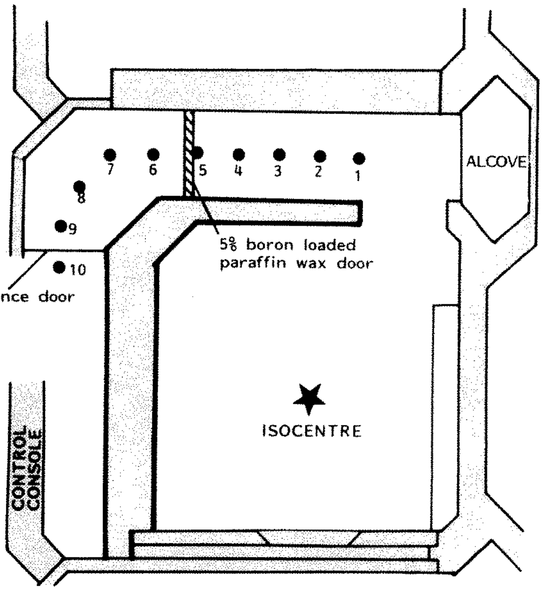

Figure 1. Maze neutron attenuation positions of measurement.

prompt capture gamma rays and X-ray leakage was measured to be 2.3 μSv/h. This corresponds to a weekly equivalent dose rate of 9.2 μSv/week. To indicate the likely proportion of this dose rate owing to capture gamma rays, the dose rate was also monitored for the 6 MV beam. At these photon energies most of the X-ray scatter interactions are via the Compton process, so one would not expect a great deal of difference between the two dose rates, were it not for the presence of prompt capture gammas.

The photon dose contribution was measured to be 17 times greater for the 24 MV beam than for the 6 MV beam. This indicates that most (~94%) of the photon leakage at the entrance door for the 24 MV beam is due to neutron capture gamma rays.

Dose due to exposure from decay of neutron activation products. Owing to the presence of neutrons whilst the accelerator is operating in the 24 MV mode, the nuclei of the various constituent atoms of concrete and materials of the accelerator capture some of these neutrons, usually emitting a prompt capture gamma ray, and become radioactive.

Decay of these neutron activation products was observed in the room after a 1 min (typical treatment time) exposure with a 24 MV photon beam dose rate of 300 cGy/min. By integrating the decay information with respect to time from 0 to 9 min (mean expected radiographer stay time in the room per patient) the dose received from a single 1 min patient exposure was estimated to 0.38 μSv. If the radiographer was to enter the room 48 times/day 5 days/week (*i.e.* workload at 24 MV of 72 000 cGy/week) then the weekly expected dose would be 91.2 μSv/week. This result is comparable with results of previous work (Tochilin & LaRiviere, 1979). Tochilin and LaRiviere (1979) identified the two dominant neutron activation products, Al ($t_{1/2}=2.3$ min) and Na($t_{1/2}=15$ h). The decay information obtained at Auckland was consistent with this.

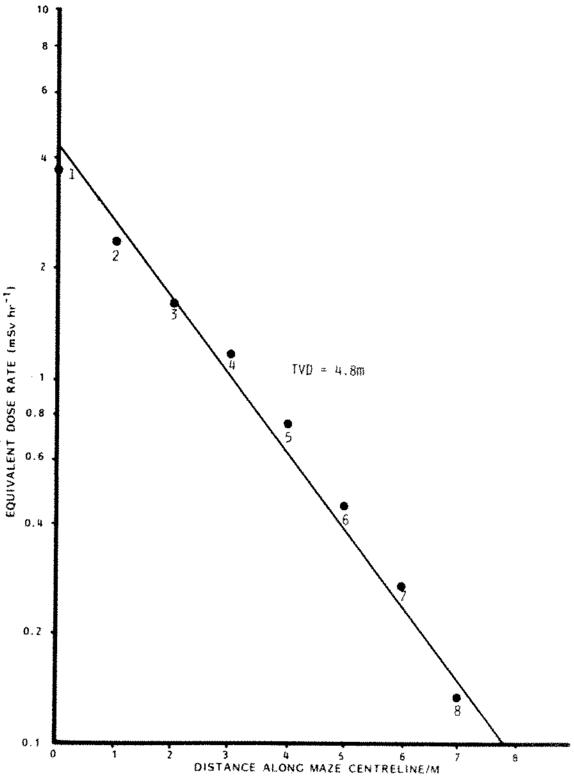

Figure 2. Equivalent dose rate attenuation of the entrance maze.

Neutron leakage equivalent dose rate. The measured neutron equivalent dose rate for the 24 MV photon beam at position 10 in Fig. 1, with the neutron doors closed was found to be 1.3 μSv/h. This is the same as a "worst case" weekly dose rate of 5.2 μSv/week.

Neutron equivalent dose rate attenuation by the entrance maze was also assessed, because this is a useful parameter for treatment room design. The graph in Fig. 2 shows the equivalent dose rate fall-off with distance travelled down the maze with the neutron doors open. From this graph a value of tenth value distance (TVD) of 4.8 m was obtained. TVD is the length of maze required to reduce the equivalent dose rate by a factor of 10. The result is in reasonable agreement with some previous work (Kersey, 1980) in which a value of approximately 5 m was observed. Kersey also presents a method for calculation of approximate neutron dose rate outside the treatment room. The method is based on two main assumptions about the attenuation of neutrons as they migrate to the entrance door. Inverse square reduction of the equivalent dose rate due to neutrons at 1 m from the target (0.17% Sv/Gy for the Clinac 2500 (Tochilin Eckert, 1986)) is assumed to the point along the maze centreline where the line of sight of the target is lost. A TVD of 5 m is assumed from this point to the outside entrance of the treatment room along the maze centreline. For the Auckland case a dose rate of 7.4 μSv/h was measured outside the room at position number 10 with the neutron doors open with a photon dose rate at the isocentre of 225 cGy/min. Using Kersey's calculation, the expected dose rate would be 49 μSv/h.

Summation of the radiographer dose contributions. It is difficult to sum mixed neutron and photon doses, owing to the differences in which both distribute dose within the body. The photons which emerge into the control areas outside the treatment room will be reasonably energetic and dose from them will be essentially to the whole body. The neutrons, on the other hand, will be expected to be of near thermal energies, and dose deposition from these tends to be more at the surface (Gibson & Piesch, 1985). However, the dose contribution from neutrons is relatively small when compared with that from all photon sources, and therefore little error would be introduced by directly summing photon and neutron doses. The maximum "worst case" expected radiography staff dose is therefore 105.6 μSv/week. It is interesting to note that the majority of staff exposure is from spending time in the treatment room being involved in patient set-up, rather than from the usual exposure from X rays being scattered down the entrance maze and transmitted through the treatment room walls. Direct exposure from neutrons is relatively low.

It is important to note that this maximum is a "worst case" estimate based on a 24 MV weekly workload of 72 000 cGy/week. Clearly this is an overestimate for a dual energy photon machine (not to mention the six electron energies also). It is envisaged that the greater proportion of the machine's operation will be in electron or 6 MV modes. These modes produce negligible neutron levels and hence both dose due to neutrons, capture gamma rays and exposure from neutron activation products will be reduced accordingly. If a more realistic workload figure for 24 MV photons were considered (say 15 000 cGy/week), the expected staff radiation dose levels would be reduced to about 21 μSv/week, which is less than the expected dose due to natural background radiation. No undue radiation risk exists at the Auckland installation for routine operation.

At a large institution with a machine dedicated to high energy treatments (*e.g.* two field pelvis), the staff exposure rates may well become significant and indeed unacceptable. Some effort would have to be directed towards reducing the neutron activation of, in particular, aluminium present in concrete shielding, perhaps by using borated polyethylene tiles on the room walls; staff rotation could be used to help reduce each individual's exposure.

Neutron spectrum outside the room

The photomultiplier-based ^{6}Li glass scintillator thermal neutron detection system has essentially zero response to other than thermal neutrons (Nuclear Enterprises, 1984). As a result one would expect the two detector systems to agree, assuming that all neutrons outside the treatment room were thermalized. When the test was done the thermal neutron system gave a result that was five times lower than the rem-meter. In fact, other workers (Muller-Runkel et al, 1986) have measured the neutron spectrum outside a Therac 20 accelerator room and found that the spectrum consisted of two peaks: one thermal peak and another peak centred at about 200 keV. The 200 keV peak contributed five times more to the equivalent dose than the thermal peak. This could explain the differences in the meter readings at Auckland. Without access to neutron spectroscopy equipment this could not be conclusively verified.

Conclusions

Dose contribution to staff is dominated by exposure to gamma rays from neutron-activated Al present in the concrete shielding. This is something which should be borne in mind in design of such a facility. Neutron production has a number of indirect effects which may not be immediately obvious.

During machine maintenance it may well be that work has to be carried out on components that are subject to the intense high energy photon beam. It should be remembered that these could be sources of radiation due to neutron activation products. The use of a Geiger Muller survey meter is advised during such work in order that the potentially radioactive components can be treated with the appropriate care.

Acknowledgments

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References

Beckham, W. A. & Entwistle, R. F., 1987. Neutron doses to personnel from a 24 MV betatron. *Australasian Physical and Engineering Sciences in Medicine*, *10*(3), 167–170.

Fox, J. G. & McAllister, J. D., 1977. Fast neutrons from a 25-MeV betatron. *Medical Physics*, *4*(5), 387–396.

Gibson, J. A. B. & Piesch, E., 1985. *Neutron Monitoring for Radiological Protection* (International Atomic Energy Agency, Vienna).

Ing, H. & Shore, R. A., 1982. Unwanted radiation produced by leakage neutrons from medical electron accelerators. *Medical Physics*, *9*(1), 34–36.

Kersey, R. W., 1980. *The Estimation of Neutron and Gamma Radiation Doses in the Entrance Mazes of SL75-20 Treatment Rooms (Publication 1127-2)* (M.E.L., Crawley, England (a division of Philips Electronics and Associated Industries Limited)).

LaRiviere, P. D., 1985. Neutron sources in a 24-MV medical linear accelerator. *Medical Physics*, *12*(6), 806–809.

Muller-Runkel, R., Ovadia, J., Culbert, H., Cooke, R. H. & Dolecek, E. H., 1986. The neutron dose and energy spectrum outside a 20-MV accelerator treatment room. *Medical Physics*, *13*(5) 742–747.

Nuclear Enterprises Ltd., 1984. *Scintillators for the Physical Sciences* (Brochure).

Palta, J. R., Hogstrom, K. R. & Tannanonta, C., 1984. Neutron leakage measurements from a medical linear accelerator. *Medical Physics*, *11*(4), 498–501.

Tochilin, E. & LaRiviere, P. D., 1979. Neutron leakage characteristics related to room shielding. In *NBS Special Publication 554* (Proceedings of a conference on neutrons from electron medical accelerators held at the National Bureau of Standards, Gaithersburg, Maryland, USA, April 9–10, 1979).

Tochilin, E. & Eckert, C., 1986. *Varian Annual Leakage Survey for Clinac 2500 SN 017* (Varian RAD-PA-6-0145).

Case reports

Mammographic depiction of Poland's syndrome

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Poland's syndrome is a group of congenital anomalies of the chest wall, with or without involvement of the ipsilateral upper extremity. We present the first case of Poland's syndrome diagnosed by mammography and the first example of Poland's syndrome in the mammographic literature.

Case report

A 39-year-old woman with *in situ* carcinoma of the cervix was noted, on physical examination, to have a small right breast with fullness in the upper outer quadrant of that breast. A subsequent mammogram shows a hypoplastic right breast and absence of the right pectoralis major muscle (Fig. 1). The patient was unaware of her anomaly.

Discussion

Poland's syndrome is named after Alfred Poland, who, in 1841, described the cadaveric dissection of a 27-year-old man with absence of the sternocostal portion of the pectoralis major, absence of the pectoralis minor, and malformations of the ipsilateral hand.

Over 400 subsequent cases of Poland's syndrome, with varying degrees of involvement of the ipsilateral upper extremity, have been reported. The right side is involved twice as often as the left side (Hopper et al, 1985). Most authors state a 3:1 male:female predominance. However, Seyfer et al (1988) describe the syndrome in 25 women and only eight men in their report on 33 patients.

The most common congenitally absent muscles are the pectoralis major and minor (Demos et al, 1985), usually partial, occurring with a minimum frequency of 1/16 500 live births (Beals & Crawford 1976). Complete absence of the pectoralis major is rare. Many patients have partial absence of the pectoralis without abnormalities of the hand (Holmstrom et al, 1986).

The etiology of Poland's syndrome is thought to be an intrauterine insult rather than a genetic defect. Goldberg and Mazzei (1977) propose that a localized insult occurs in the seventh week of gestation, when the developing limb bud is adjacent to the chest wall and the hand is undergoing changes in the web spaces and middle phalangeal formation. The insult may be hypoxic, possibly owing to arterial spasm or arterial malformation. David (1972), in 10 cases, found a high frequency of adoption, attempted abortion, or unwanted pregnancy. This suggests that a uterine insult, such as hypoxia or exposure to a toxin, may have contributed to the genesis of Poland's syndrome.

In addition to the absence of the sternocostal portion of the pectoralis major muscle and hypoplasia of the breast, as occurred in our patient, many other abnormalities have been described in association with Poland's syndrome. These include the following: absence or hypoplasia of the pectoralis minor, external oblique, latissimus dorsi or serratus anterior muscles; skeletal abnormalities such as the absence or hypoplasia of one or more ribs (occasionally with lung herniation) or of any bone of the ipsilateral upper extremity, syndactyly or brachydactyly and Sprengel's deformity; cutaneous abnormalities including the absence of the nipple, webbing of the axilla or fingers and decreased subcutaneous tissue; genitourinary abnormalities; and hematologic abnormalities including acute leukemia.

Finally, this case illustrates that while the breast may merely appear to be small because of absence of the

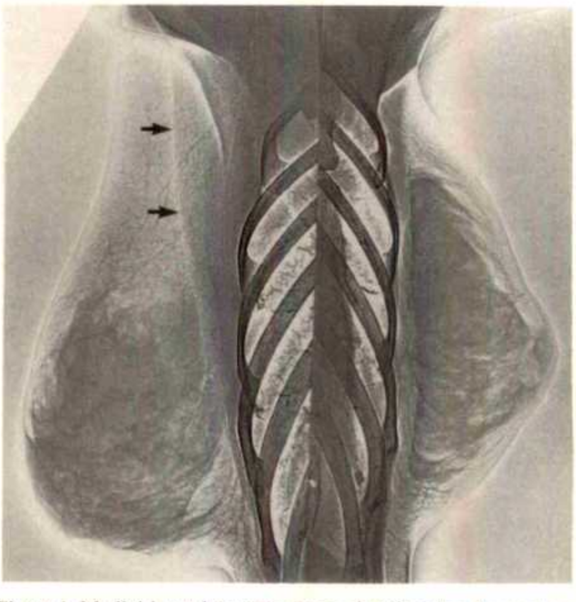

Figure 1. Medial-lateral mammograms showing that the pectoralis muscle (arrows) is present only on the left side. The right breast is hypoplastic.

underlying pectoralis major, true breast hypoplasia may exist.

References

Beals, R. K. & Crawford, S., 1976. Congenital absence of the pectoral muscles. A review of twenty-five patients. *Clinical Orthopedics*, *119*, 166–171.

David, T., 1972. Nature and etiology of the Poland anomaly. *New England Journal of Medicine*, *287*, 487–489.

Demos, T., Johnson, C., Love, L. & Posniak, H., 1985. Computed tomography of the partial unilateral agenesis of the pectoralis muscles. *Journal of Computerized Axial Tomography*, *9(3)*, 558–559.

Goldberg, M. & Mazzei, R., 1977. Poland syndrome: a concept of pathogenesis based on limb bud embryology. *Birth Defects*, *13*, 103–115.

Holmstrom, H., Suurkula, M. & Lossing, C., 1986. Absent latissimus dorsi muscle and anhidrotic axilla in Poland's syndrome. *Scandinavian Journal of Plastic and Reconstructive Surgery*, *20*, 313–318.

Hopper, K., Haas, D., Rice, M., Freeley, D., Taubner, R. & Ghaed, N., 1985. Poland–Mobius syndrome: evaluation by computerized tomography. *Southern Medical Journal*, *78(5)*, 523–527.

Poland, A., 1841. Deficiency of the pectoralis muscle. *Guy's Hospital Reports*, *6*, 191–193.

Seyfer, A., Icochea, R. & Graeber, G., 1988. Poland's anomaly. *Annals of Surgery*, *208(6)*, 776–782.

Spontaneous disappearance of tuberculous psoas abscess calcification

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(Received July 1989)

Calcified psoas abscesses are a characteristic feature of tuberculosis of the thoraco-lumbar spine. We present a case in which well established calcification has almost completely disappeared, several years after any anti-tuberculous treatment. A review of the English literature has revealed no previous report of this finding.

Case report

The patient, now a 48-year-old woman, first presented at the age of 6 with back pain and radiographic features of spinal tuberculosis at T12/L1. Bilateral calcified psoas abscesses developed over the next few months. Management was first by bed rest and later, at the age of 12, by postero-lateral drainage with spinal fusion. By this time abscess calcification was well established. The patient then remained relatively well until the age of 33, when she developed girdle pain due to further vertebral destruction at a higher level (T8–T12).

This new focus was drained via a trans-thoracic approach and a small abscess cavity was found which did not communicate with the original psoas abscesses. *Tubercle bacilli* were cultured. Radiographs of the lumbar spine at this time still showed a large calcified psoas abscess on the right side and a small one on the left. Appropriate antibiotic cover was given for 2 years until 1975 when it was noted that the calcification in the left psoas abscess had decreased. Routine follow-up radiographs in 1981 (Fig. 1) still showed calcification in both psoas abscesses but subsequent films (Fig. 2) have shown a dramatic reduction in calcification at a time when the patient had not received any anti-tuberculous treatment for many years. During this time, the patient remained well, apart from symptoms due to the menopause, for which she was given a short course of hormone replacement therapy.

Discussion

Psoas abscess formation has been reported in up to 12% of cases of spinal tuberculosis (Seddon et al, 1973).

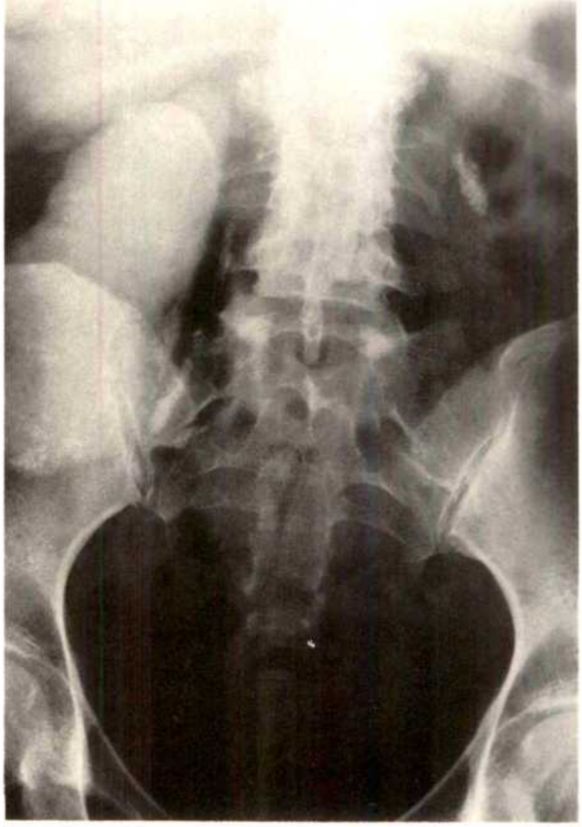

Figure 1. Bilateral psoas abscess calcification on a radiograph taken in 1981, 6 years after any anti-tuberculous treatment.

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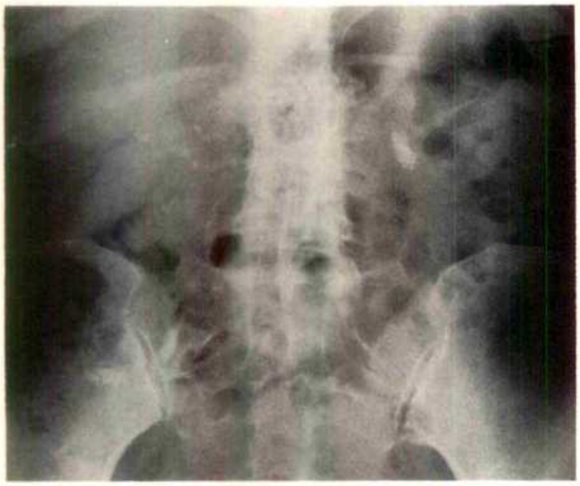

Figure 2. A radiograph taken in 1989 showing bilateral psoas abscesses but the calcification, particularly on the right side, is considerably less.

Calcification commonly occurs, and without intervention remains static.

The mechanism whereby the calcification has cleared in our patient is uncertain. Theoretically, spontaneous reduction in the amount of observed calcification could occur if a fistula developed, and intestinal perforation by a tuberculous psoas abscess has been reported (Blumenthal et al, 1981). However, no evidence for this was seen in our patient. At no time did either abscess contain air, and there has been no disturbance of bowel function. Similarly, surgical or percutaneous drainage of an abscess could also cause a reduction in the amount of calcification, but no such intervention was undertaken. Furthermore, colleagues who have had considerable experience in the field of spinal tuberculosis cannot recall seeing such an event (Griffiths, 1988; Murray, 1988).

References

BLUMENTHAL, D. H., MORIN, M. E., TAN A. & LI, Y. P., 1981. Intestinal penetration by tuberculous psoas abscess. *American Journal of Roentgenology*, *136*, 995–997.

GRIFFITHS, D. LL., 1988. Personal communication.

MURRAY, R. O., 1988. Personal communication.

SEDDON, H. ET AL, 1973. Medical Research Council Working Party on Tuberculosis of the Spine, Second Report. *Tubercle*, *54*, 261–282.

Osteosarcoma: an unusual thoracic metastasis

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(*Received July 1989*)

Metastases from osteosarcoma often occur in the lungs, usually as multiple nodules but sometimes as a solitary mass. Lymph node involvement is unusual. We present a case of metastatic recurrence as a solitary, stellate, ossified, pulmonary mass extending across the pleura associated with ossified hilar lymphadenopathy.

Case report

A 15-year-old male, whose only previous medical history was resection of a right ventricular infundibular stenosis 18 months earlier, presented in November, 1987 with pain and swelling in the distal right femur. This proved on biopsy to be caused by an osteosarcoma, and after staging with chest radiograph, computed tomography (CT) and bone scintigraphy, no spread was evident. After three courses of cisplatinum and adriamycin, the distal femur containing the primary tumour was resected and a knee prosthesis inserted. Following three further courses of chemotherapy he remained well for nearly a year, until March, 1989. A follow-up chest radiograph at this time revealed right paratracheal lymphadenopathy and an upper lobe mass (Fig. 1). A chest radiograph 2 months earlier had been normal. Computed tomography demonstrated an irregular, stellate mass with central ossification in the right upper lobe, extending supero-posteriorly, and ossifying lymphadenopathy around the upper lobe bronchus (Fig. 2). The latter was connected to the mass by strands of ossified material. Scintigraphy with ^{99}Tc^{m}-hydroxy methylene diphosphonate (^{99}Tc^{m}-HMDP) revealed intense uptake in the mass and nodes but no skeletal metastases (Fig. 3). At thoracotomy ossified tumour was found to be invading through the pleura into the superior sulcus and was resected together with the involved nodes. Histology showed an osteoblastic osteosarcoma consistent with spread from the femoral primary.

Discussion

The lungs are the most frequent site for metastases from osteosarcomas (Jeffree et al, 1975; Weiss & Gilbert, 1978). Pulmonary nodules are seen in 10% of patients at presentation and more than 70% at death (McKenna et al, 1966). The nodules are usually multiple and bilateral but in 35% of patients may be unilateral, as in this case. The usual appearance of pulmonary metastases from any primary is of well-circumscribed, spherical nodules (Crow et al, 1981) and those from osteosarcomas may contain calcification or ossification.

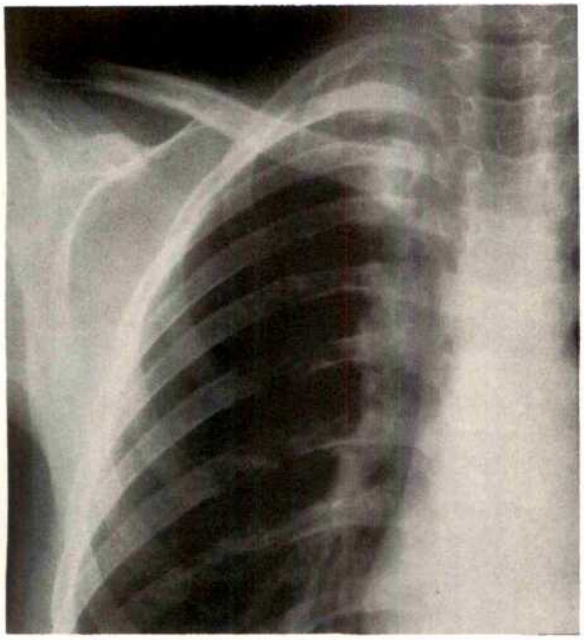

Figure 1. Chest radiograph showing right paratracheal lymphadenopathy and an upper lobe mass.

Fifty-one per cent are subpleural and may cause spontaneous pneumothorax in 5% of patients (McKenna et al, 1966), while 49% are parenchymatous (Vanel et al, 1984).

The best technique for demonstrating pulmonary deposits is CT; scintigraphy can detect only 5% of these (Vanel et al, 1984). However, scintigraphy can demonstrate metastases at many sites, usually from osteoblastic primaries.

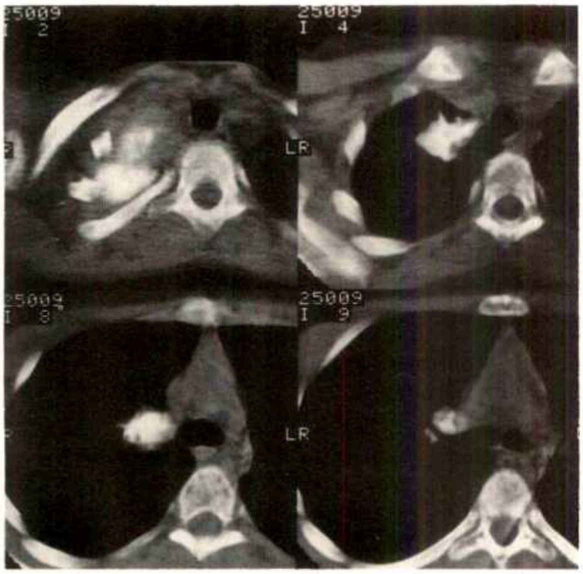

Figure 2. Computed tomographic scans demonstrating an irregular, stellate mass with central ossification in the right upper lobe extending supero-posteriorly, and ossifying lymphadenopathy around the upper lobe bronchus.

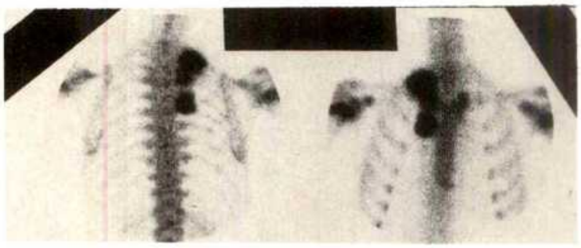

Figure 3. Posterior and anterior views shown on $^{99}\mathrm{Tc^m}$-HMDP scintigrams.

Lymph node involvement is a bad prognostic sign in osteosarcoma (McKenna et al, 1966) and is uncommon, being seen in only 3% of patients, in life (Jeffree et al, 1975). However, in the same study, 26% of cases at post-mortem had spread to local, hilar, mediastinal, mesenteric or abdominal nodes. Lymph node deposits appear more common from an osteoblastic primary (Tobias et al, 1985; Madsen, 1979) than from other histological types and can be demonstrated by scintigraphy (Heyman, 1980).

In our case the mass is unusual in that while lymph node deposits and metastatic uptake of $^{99}\mathrm{TC^m}$-HMDP are more likely with an osteoblastic osteosarcoma, a solitary, invasive, stellate metastasis has not been previously described.

Acknowledgments

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References

Crow, J., Slavin, G. & Kreel, L., 1981. Pulmonary metastasis: a pathologic and radiologic study. *Cancer*, *47*, 2595–2602.

Heyman, S., 1980. The lymphatic spread of osteosarcoma shown by Tc-99m-MDP scintigraphy. *Clinical Nuclear Medicine*, *5*, 543–545.

Jeffree, G. M., Price, C. H. G. & Sissons, H. A., 1975. The metastatic patterns of osteosarcoma. *British Journal of Cancer*, *32*, 87–107.

Madsen, E. H., 1979. Lymph node metastases from osteoblastic osteogenic sarcoma visible on plain films. *Skeletal Radiology*, *4*, 216–218.

McKenna, R. J., Schwinn, C. P., Soong, K. Y. & Higinbotham, N. L., 1966. Sarcomata of the osteogenic series (osteosarcoma, fibrosarcoma, chondrosarcoma, parosteal osteogenic sarcoma, and sarcomata arising in abnormal bone). *Journal of Bone and Joint Surgery*, *48A*, 1–25.

Tobias, J. D., Pratt, C. B., Parham, D. B., Green, A. A. & Rao, B., 1985. The significance of calcified regional lymph nodes at the time of diagnosis of osteosarcoma. *Orthopedics*, *8*, 49–52.

Vanel, D., Henry-Amar, M., Lumbroso, J., Lemalet, E.,

1990, *The British Journal of Radiology*, *63*, 306–308

COUANET, D., PIEKARSKI, J. D., MASSELOT, J., BODDAERT, A., KALIFA, C., LE CHEVALIER, T. & LEMOINE, G., 1984. Pulmonary evaluation of patients with osteosarcoma: roles of standard radiography, tomography, CT, scintigraphy, and tomoscintigraphy. *American Journal of Roentgenology*, *143*, 519–523.

WEISS, L. & GILBERT, H. A., 1978. In *Pulmonary Metastasis* (G. K. Hall & Co, Boston, USA), pp. 100–103.

Pneumonia, diagnosed on the abdominal radiograph, as a cause for acute abdomen in children

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Three cases of acute abdomen in children are described where a diagnosis of pneumonia was recorded as the cause of the abdominal pain. In each case, pulmonary consolidation was identified on the plain abdominal radiograph. The diagnostic value of plain abdominal radiographs in children is increased by deliberately including the lung bases.

Acute abdominal pain is a common cause of paediatric emergency referral and admission to hospital. Acute appendicitis is the most common identifiable organic cause (Drake, 1980). Extensive lists can be made of other possible causes (Table I), and investigations are directed to reaching a working diagnosis within a few hours of admission.

I report three recent cases of acute abdominal pain in children in which pneumonia was diagnosed as the cause of the pain. In each case, the diagnosis was suggested by identifying pulmonary consolidation on the plain abdominal radiograph.

Table I. Important causes of acute abdominal pain in children

Non-specific abdominal pain	
Gastrointestinal:	Appendicitis Constipation Mesenteric adenitis Intestinal obstruction Gastroenteritis Hepatitis Henoch–Schonlein purpura Inflammatory bowel disease Inflamed Meckel's diverticulum Pancreatitis
Genito-urinary:	Infection Calculus Reflex Hydronephrosis Torsion of testis
Diabetic ketoacidosis	
Gynaecological	
Pneumonia	
Porphyria	
Trauma	

Case reports

Case 1

A 10-year-old girl was admitted with a 4 day history beginning with a sore throat which had settled after 24 hours.

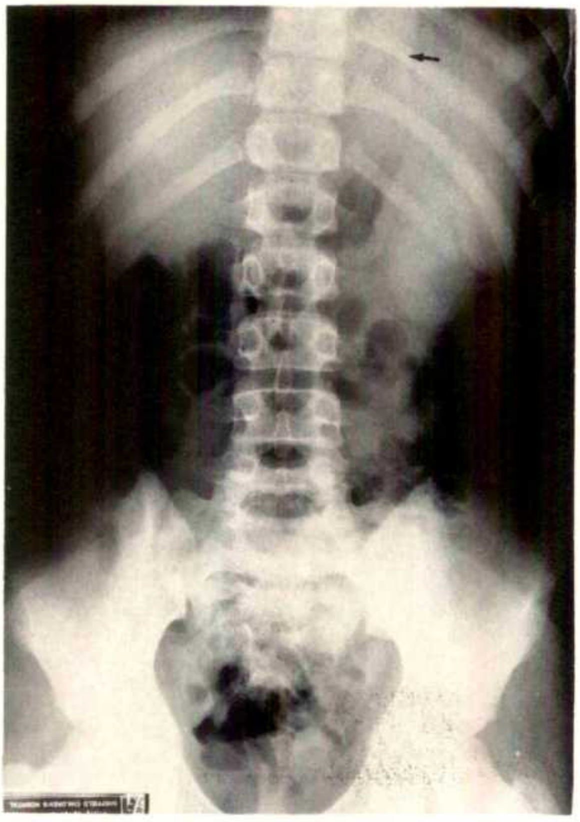

Figure 1. Case 1. Plain abdominal radiograph including the lung bases and revealing changes consistent with consolidation.

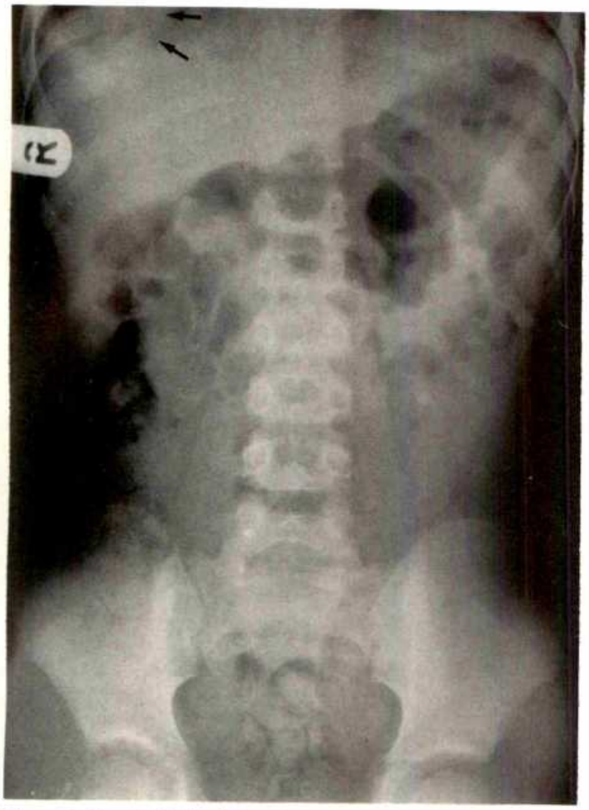

Figure 2. Case 2. Plain abdominal radiograph showing consolidation at the base of the right lung.

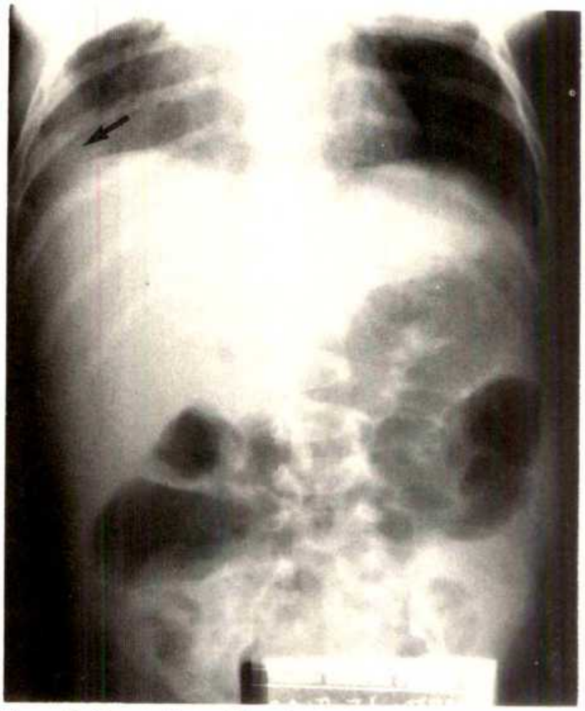

Figure 3. Case 3. Plain abdominal radiograph showing patchy consolidation in the right lower lobe.

Subsequently, she developed a cough and constant central abdominal pain with vomiting. There was frequency of micturition, but no dysuria. On examination she was pyrexial to 39.2°C and had cervical lymphadenopathy. Her ears and throat were normal, a tachycardia of 150 was recorded and her chest was clear on auscultation. Examination of her abdomen revealed tenderness in the left upper quadrant, but it was otherwise generally soft with normal bowel sounds. The differential diagnosis was thought to lie between pyelonephritis or mesenteric adenitis. A mid-stream urine specimen was normal. A plain abdominal radiograph was taken (Fig. 1); the bases of the lungs were included and revealed changes consistent with consolidation. A subsequent chest radiograph confirmed left lower lobe pneumonia. Antibiotic treatment was started and the girl made a full and uneventful recovery.

Case 2

A 5-year-old boy was referred to the Accident and Emergency Department with a history of having awoken in the night crying and complaining of abdominal pain. He subsequently settled but in the morning complained again of constant central abdominal pain increased by coughing. He did not vomit, and there was no dysuria. On examination his temperature was 37.5°C. There was no lymphadenopathy. His respirations were rapid and shallow but his chest was clear on auscultation. There was tenderness in the right iliac fossa, although his abdomen was soft. Rectal examination showed right-sided tenderness, and urine examination was normal. A diagnosis of acute abdomen, possibly due to acute appendicitis, was made and the child was referred for a paediatric surgical opinion. A plain abdominal radiograph was taken and this showed consolidation at the base of the right lung (Fig. 2). A right lower lobe pneumonia was confirmed on the subsequent chest radiograph. Following antibiotic treatment, the patient made a full recovery.

Case 3

A 2-month-old baby was referred to casualty with apparent abdominal pain and vomiting. There was a 3 day history of vomiting, poor sleeping and restlessness. This had been accompanied by crying and drawing up of the legs. For 2 days the motions had been loose with occasional diarrhoea, but by admission this had resolved. On examination the baby looked unwell, was crying and drawing up his legs. He was pyrexial to 37.4°C. Mild cervical lymphadenopathy was present. Respiratory rate was 44, but the chest was clear on auscultation. Abdominal examination was unremarkable. In view of the apparent abdominal pain the child was referred for a surgical opinion. A plain abdominal radiograph was taken which showed patchy consolidation in the right lower lobe (Fig. 3). This was confirmed on the chest radiograph. With antibiotic therapy, the baby made a rapid recovery. Further investigation after a second chest infection revealed significant gastro-oesophageal reflux.

Discussion

The child with acute abdominal pain is a difficult diagnostic problem. Indeed, the largest diagnostic group is that of non-specific abdominal pain (Jones, 1969; Drake, 1980; Dickson et al, 1988). Young children find it more difficult to localize the pain than adults, therefore it is important to consider the whole child and not

1990, *The British Journal of Radiology*, *63*, 308–310

confine attention to the abdomen. A working diagnosis must be reached as soon as possible and achieved by a careful clinical assessment which is repeated often after a short period of time (Jackson, 1963; Jones, 1976). Investigation will include urine analysis, and a plain abdominal radiograph may be taken, particularly if a clinical diagnosis is not apparent. Although a valuable investigation for demonstrating a radio-opaque faecolith, intestinal obstruction or intussusception, in one large series the abdominal radiograph did not suggest a diagnosis which was not clinically suspected (Drake, 1980). In the cases of acute abdominal pain described here, the plain abdominal radiograph suggested the diagnosis, which was not apparent on the initial clinical assessment, as a result of including the lung bases.

Lower lobe pneumonia accounts for between 2% and 5% of causes of acute abdominal pain in children (Winsey & Jones, 1967; Jona & Belin, 1976; Jones, 1976; Sims & Alexander, 1976). Although tachypnoea of peritonitis is recognized, a raised respiratory rate should provide a clue to the correct diagnosis, even in the absence of chest signs. Dominance of abdominal symptoms over the thoracic findings is not unusual. It has been recommended that a chest radiograph including a lateral view be taken in all children presenting with an acute abdomen, irrespective of whether an abdominal radiograph is taken (Jona & Belin, 1976; Anon, 1976). Since pneumonia accounts for only 2.5% of causes of acute abdominal pain, few would wish to incur this extra irradiation to the child and extra cost. It is, therefore, not usual paediatric practice to take radiographs of the chest or the abdomen as a routine in all cases of abdominal pain. This report suggests that, in cases of clinical uncertainty where a plain abdominal radiograph is taken, the diagnostic value of this can be increased by including the lung base. The report also stresses the importance of not confining attention to the areas below the diaphragm when viewing an abdominal radiograph.

Acknowledgments

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References

Anon, (1976). Children with appendicitis. *British Medical Journal*, *ii*, 440–441.

Dickson, J. A. S., Jones, A., Telfer, S. & de Dombal, F. T., 1988. Acute abdominal pain in children. *Scandinavian Journal of Gastroenterology*, *23*, *Suppl. 144*, 43–46.

Drake, D. P., 1980. Acute abdominal pain in childhood. *Journal of the Royal Society of Medicine*, *73*, 641–645.

Jackson, R. H., 1963. Parents, family doctors and acute appendicitis in childhood. *British Medical Journal*, *ii*, 277–281.

Jona, J. Z. & Belin, R. P., 1976. Basilar pneumonia simulating acute appendicitis in children. *Archives of Surgery*, *iii*, 552–553.

Jones, P. F., 1969. Acute abdominal pain in childhood with special reference to cases not due to acute appendicitis. *British Medical Journal*, *ii*, 284–286.

Jones, P. F., 1976. Active observation in management of acute abdominal pain in childhood. *British Medical Journal*, *ii*, 551–553.

Sims, D. G. & Alexander, F. W., 1976. Acute abdominal pain in childhood. *British Medical Journal*, *ii*, 880–881.

Winsey, H. S. & Jones, P. F., 1967. Acute abdominal pain in childhood: analysis of a year's admissions. *British Medical Journal*, *i*, 653–655.

Congenital indifference to pain mistaken for non-accidental injury

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(*Received July 1989*)

Congenital indifference to pain is a rare autosomal recessive inherited condition with cutaneous and skeletal lesions that mimic non-accidental injury (NAI). We present this case to illustrate the difficulty in differentiating the two conditions in early childhood and to demonstrate discriminatory features in the older child.

Case report

The affected boy, born in the UK to Pakistani parents, first came to medical attention aged 6 months. (He had escaped the obstetric profession having been delivered by his father in the family car in the hospital car park!) When admitted to investigate recurrent chest infections, he was noted to have burns on his left hand. His parents explained that he had touched an electric heater while crawling. He was underweight, but his parents claimed that he was a poor feeder. Over a 6 month period there were several further admissions with chest infections, mainly affecting the right upper lobe. No underlying cause was found. The pneumonias resolved and were retrospectively attributed to episodes of aspiration. A further unexplained feature was recurrent oral and labial ulceration including one deep lesion on the tongue.

At 18 months of age he was taken to the Accident Department by his parents who had noticed a boggy mass over his occiput. An occipital fracture was present (Fig. 1). No explana-

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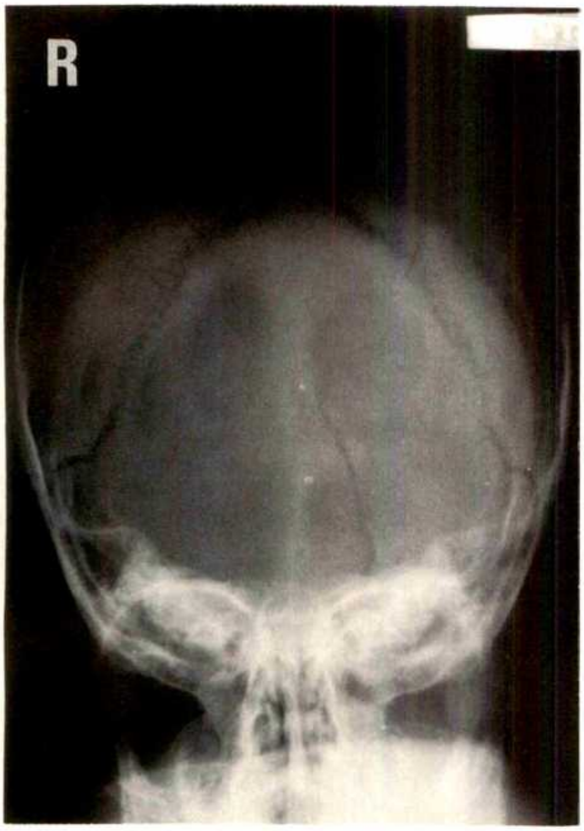


Figure 1. Skull radiograph showing a linear occipital fracture.

tion was offered by his parents. Further suspicion of non-accidental injury (NAI) was raised by burns on the fingers of the right hand, deep cuts to both index fingers and a number of bruises about the trunk and limbs (Fig. 2). One revealing note by the admitting physician was his father's comment that the child was always running into things but never cried. This admission was following by a case conference under the Child Abuse Procedures at which close supervision by his GP and community services were urged.

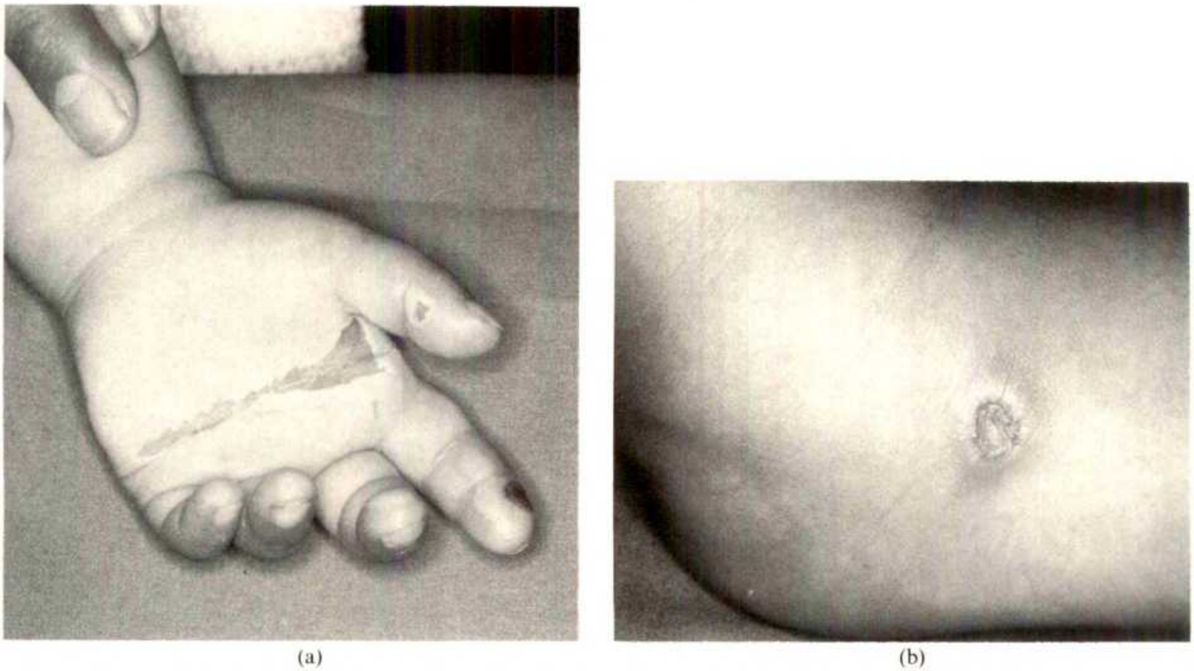
Six months later he was admitted at the request of his GP with a fresh burn to his left hand. His teeth were rotten and his tongue and lips ulcerated. He was accompanied by his 16-year-old step-sister whose heated iron he had been discovered touching, apparently without pain. This crucial information was followed by provocative sensory testing on the ward which confirmed a lack of response to painful stimuli but showed normal tactile sensation.

After assessment at the Great Ormond Street Hospital for Sick Children, he was diagnosed as having a hereditary sensory neuropathy with loss of pain and temperature sensation. Detailed electrophysiological studies and electron-microscopy suggested similarities with another Asian kindred. In his family in Pakistan, one cousin aged 4 years has been found to have similar clinical features. Another, who died aged 5 years, is strongly suspected of having been affected. All three cases involve first cousin marriages within the same extended family.

A further case conference was held in an attempt to advise the family on how to protect him from self harm. This appears to have been partially successful. Now in his first year at school, he was recently seen by his GP with swollen knees following a fall in the playground. Knee radiographs were requested (Fig. 3).

Discussion

The bizarre skeletal manifestations in early childhood of congenital indifference to pain result both from



(a)

(b)

Figure 2. Clinical photographs of burns to the right hand and right foot, in (b) similar to a cigarette stubbing injury.

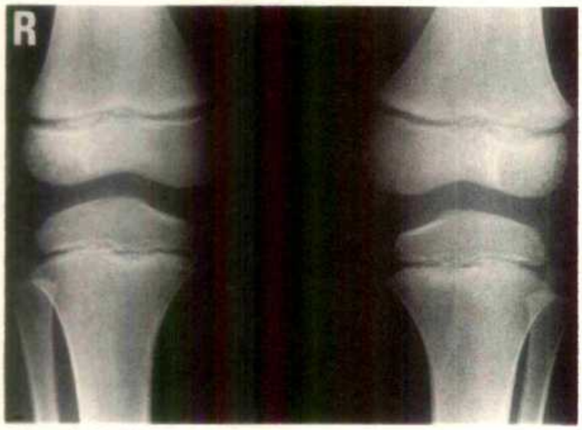


Figure 3. Radiograph of the knees at 5 years of age. In addition to aseptic necrosis of the lateral femoral condyles, there is growth plate widening in the distal femora.

episodes of major trauma (which may go unrecognized) and from repeated microtrauma. In addition, various forms of osteomyelitis occur (Murray, 1957; Silverman & Gilden, 1959). The Charcot-type joints of other neuropathic conditions are not manifest until later childhood (Siegelman et al, 1966). In infancy cortical thickening is seen in the long bones as a result of repeated sub-periosteal haemorrhage. Metaphyseal injuries may also be found. An almost identical pattern of injuries was described contemporaneously with NAI (Caffey, 1957). When associated with the burns and other cutaneous and oral results of self mutilation, the condition may be extremely difficult to differentiate from NAI.

In slightly older children after walking commences, there are repeated episodes of microtrauma resulting in areas of aseptic necrosis and osteochronditis in the juxta-articular regions of weight bearing joints (Siegelman et al, 1966). The lateral femoral condyle is particularly affected in contrast to the usual medial sites of osteochronditis dissecans in childhood and aseptic necrosis in the adult (Murphy, 1986). This difference is unexplained but may reflect unusual stresses consequent upon the feats of valour that affected children are prone to perform such as jumping or diving from heights. Joint deformity and swelling may also result from epiphyseal plate injury and even displacement (Murray, 1957). Widening of the growth plate (Siegelman et al, 1966) may also cause confusion with NAI.

The clinical features of congenital indifference to pain may provide helpful discriminators. Corneal opacities may result (from unrecognized ocular trauma) and the oro-labial ulceration is often out of all proportion to the skeletal manifestations. The history provided by parents and siblings, as with suspected NAI, may also give vital clues. Affected individuals are noted not to cry after corporal punishment (Murray, 1957). Conversely, one mother was reported to have cried from the pain of hitting her affected child (Silverman & Gilden, 1959). In his editorial footnote to this article, Felson remarks that the condition gives a new twist to the old saying "this hurts me more than it does you".

Acknowledgments

We would like to thank Dr J. Connel for permission to report this case and Dr D. Lindsell for his helpful advice.

References

CAFFEY, J., 1957. Some traumatic lesions in growing bones other than fractures and dislocations: clinical and radiological features. *British Journal of Radiology, 30*, 225–238.

MURPHY, W. A., 1986. In *Diagnostic Radiology*. Ed. by R. G. Grainger & D. J. Allison (Churchill Livingstone, Edinburgh), pp. 1473–1508.

MURRAY, R. O., 1957. Congenital indifference to pain with special reference to skeletal changes. *British Journal of Radiology, 30*, 2–10.

SIEGELMAN, S. S., HEIMANN, W. G. & MANIN, M. C., 1966. Congenital indifference to pain. *American Journal of Roentgenology, 97*, 242–247.

SILVERMAN, F. N. & GILDEN, J. J., 1959. Congenital insensitivity to pain: a neurologic syndrome with bizarre skeletal lesions. *Radiology, 72*, 176–189.

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Case of the month

A diaphragmatic nick

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(*Received January 1989*)

A 27-year-old man was admitted with acute onset of severe, constant epigastric pain and vomiting associated with lifting at work. There were no other symptoms. Four years previously he had attended the Casualty Department with a knife wound to the left chest which had been sutured. Examination revealed only generalized abdominal tenderness. Haematological and biochemical investigations showed a mildly elevated white cell count (16.1×10^9/L). Abdominal radiographs were unremarkable. Forty-eight hours after admission he deteriorated rapidly with increasing abdominal pain, hypotension and tachycardia.

Figures 1 and 2 show chest radiographs on admission and at 48 hours. Figure 3 shows an ultrasound examination of the left thorax at the time of the second chest radiograph. What diagnosis do you suspect and how might this be confirmed?

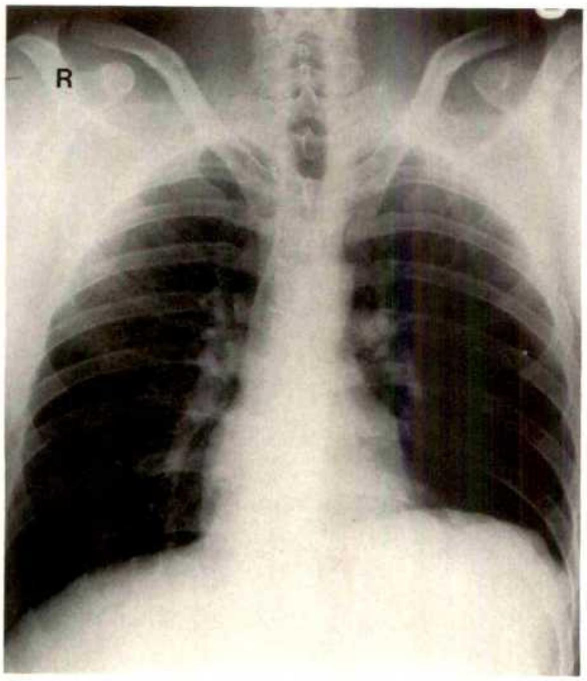

Figure 1. Chest radiograph on admission.

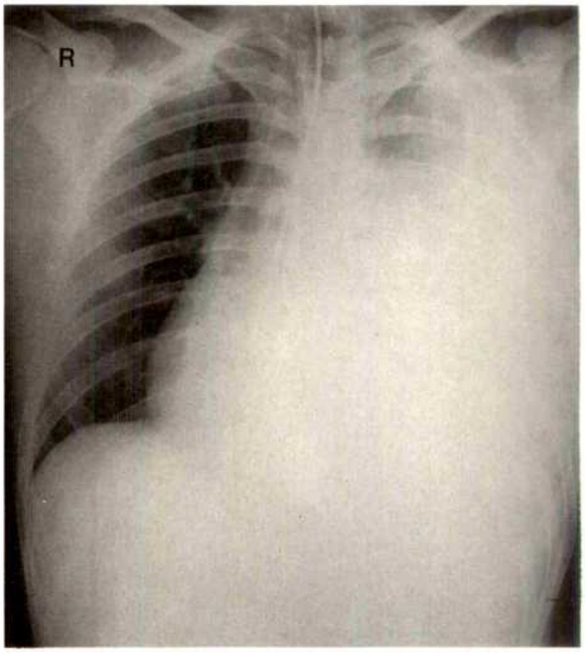

Figure 2. Chest radiograph 48 hours after admission.

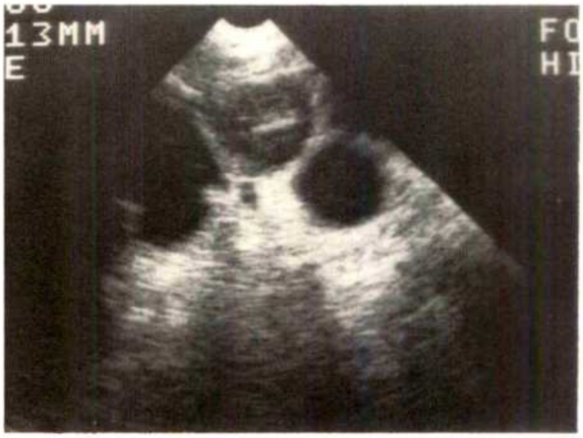

Figure 3. Transverse ultrasound scan of the left lower thorax.

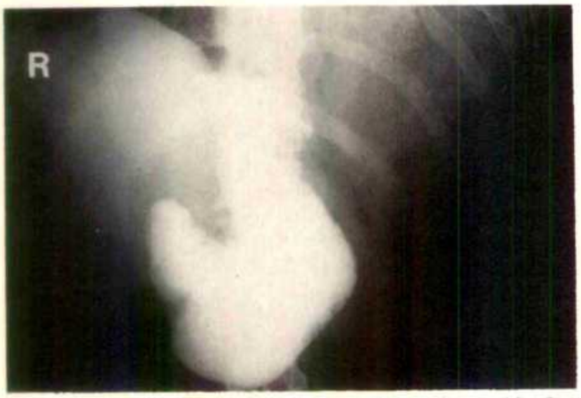

Figure 4. Radiograph of upper abdomen/lower thorax 4 h after administration of water-soluble contrast medium.

The radiographs show a slightly elevated left hemi-diaphragm with an irregular contour (Fig. 1) and a large pleural effusion with contralateral mediastinal shift (Fig. 2). The ultrasound demonstrates multiple rounded fluid-filled structures in the thorax which showed peristalsis. A further, non-motile, rounded structure with hypoechoic rim and linear echogenic centre can also be identified. These structures were felt to represent small bowel and colon respectively. A diagnosis of diaphragmatic rupture with herniated bowel was made, confirmed by a water-soluble contrast examination of the upper gastro-intestinal tract. A radiograph at 4 h (Fig. 4) shows the stomach displaced to the right and failure of the contrast medium to progress beyond the duodenum indicating obstruction. The patient's condition had necessitated insertion of a left intercostal drain with subsequent drainage of three litres of haemoserous fluid, and air-containing structures are now identified in the left hemi-thorax.

At laparotomy, a four finger breadth defect was found in the left hemi-diaphragm. The left thorax contained the distal half of the transverse colon, the distal two-thirds of small bowel and omentum. The small bowel was strangulated but improved in appearance upon reduction into the peritoneal cavity. Bowel resection was therefore avoided.

Traumatic diaphragmatic rupture with subsequent herniation of abdominal organs may be caused by blunt injury, penetrating injury such as gunshot and stab wounds, or iatrogenic trauma. The left hemi-diaphragm is more frequently ruptured than the right. Healing of diaphragmatic tears may be prevented by the pleuro-peritoneal pressure gradient drawing omentum and viscera into the defect. Blunt trauma generally produces large defects often leading to early herniation of abdominal organs. Penetrating trauma may produce smaller defects which are readily occluded by omentum, preventing early herniation. If the diagnosis is not made in the acute period after the trauma, the patient enters a latent phase of variable duration which may be terminated by the onset of the obstruction/strangulation phase. Although this progression may follow any type of trauma it most commonly occurs with small defects which readily compress and compromise the vascular supply of herniated viscera (Carter et al, 1951; Grimes, 1974).

Stab wounds account for up to 88% of all such patients with delayed presentation. This group pose a difficult diagnostic problem. The trauma may have been disregarded or forgotten; additionally, clinical and radiological findings vary according to the viscera herniated and presence or absence of obstruction, strangulation or gangrene. Stomach and colon are most frequently herniated, followed by omentum, small bowel, spleen and liver. Mortality is 20% in the obstruction/strangulation phase, increasing to 80% if gangrene is present (Hegarty et al, 1978; Payne & Yellin, 1982).

With delayed presentation, physical signs are minimal unless herniation occurs. There may be rapid deterioration with cardio-respiratory embarrassment caused by distension of intra-thoracic gut and the development of a pleural effusion. Evidence of gastro-intestinal obstruction or haemorrhage suggest incarceration of viscera. Radiological findings include diaphragmatic elevation and abnormal contour, lung atelectasis, pleural effusion, intra-thoracic, air-fluid containing viscera, contralateral mediastinal shift and evidence of gastro-intestinal obstruction (Carter et al, 1951; Grimes, 1974; Payne & Yellin, 1982).

However, an air-filled viscus within the thorax can simulate diaphragmatic eventration or even pneumothorax. The herniated organ may contain no gas, appearing as a basal opacity, or the development of a large pleural effusion secondary to strangulation may obscure herniated viscera. Abdominal radiographs may show no evidence of dilated bowel if the stomach alone is herniated or if most of the involved viscera lie in the thorax (Carter et al, 1951; Grimes, 1974).

Plain radiographs and contrast media studies of the gastro-intestinal tract are generally diagnostic (Carter et al, 1951; Hegarty et al, 1978; Payne & Yellin, 1982). Ultrasound is a useful alternative examination capable of identifying intra-thoracic bowel and delineating the diaphragm, and may be used in patients who are too ill to attend the department for contrast media studies (Ammann et al, 1983). It may help diagnosis in the presence of a large pleural effusion obscuring herniated bowel without plain radiographs or contrast media studies.

References

AMMANN, A. M., BREWER, W. H., MAULL, K. I. & WALSH, J. W., 1983. Traumatic rupture of the diaphragm: real-time sonographic diagnosis. *American Journal of Roentgenology*, *140*, 915–916.

CARTER, B. N., GIUSEFFI, J. & FELSON, B., 1951. Traumatic diaphragmatic hernia. *American Journal of Roentgenology*, *65*, 56–72.

GRIMES, O. F., 1974. Traumatic injuries of the diaphragm. *American Journal of Surgery*, *128*, 175–181.

HEGARTY, M. M., BRYER, J. V., ANGORN, I. B. & BAKER, L. W., 1978. Delayed presentation of traumatic diaphragmatic hernia. *Annals of Surgery*, *188*, 229–233.

PAYNE, J. H. & YELLIN, A. E., 1982. Traumatic diaphragmatic hernia. *Archives of Surgery*, *117*, 18–24.

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Short communication

Medicolegal aspects of medical radiation exposure*

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(*Received October 1989*)

It is well known that untoward events may follow the exposure of human beings to ionizing radiations. As some such events may ensue after medical (in addition to other) exposures, it is appropriate to consider possible resultant legal complications of medical radiation exposures.

The contents of this communication are based on practice in the UK, and concentrate on those aspects of the subject which relate to the direct effects of ionizing radiation, to the exclusion of such important aspects such as the "chemical" effects of contrast media and the "mechanical" effects of interventional radiology. It is fully recognized that those two aspects are almost wholly responsible for the unenviable position of radiology (including both diagnostic radiology and nuclear medicine), high in the league table of specialities causing problems for the medical defence bodies. In recent years there have been very few examples in diagnostic radiology related to dose, except in pregnancy, though very many in the other categories. In therapy there have been few cases at all, and not all associated with dose.

Discussion is based on the following premises:

(i) that any medical radiation is expected to benefit the patient, by assisting in making a diagnosis, whether positive or negative, or by treating, though not necessarily curing, a lesion; for this reason exposure is not included in the assessment of maximum permissible dose under the Ionising Radiation Regulations, 1985,
(ii) that any such exposure will be conducted "professionally", using the best available technique and apparatus, and the minimum exposure for the purpose,
(iii) that all detectable effects of radiation on tissues are harmful,
(iv) that any exposure constitutes an assault unless acceptable consent is given, and
(v) that before a medicolegal issue arises there must be a detectable, and preferably measurable, effect.

It follows:

(i) that screening of persons for the benefit of others is excluded, *e.g.* examining potential teachers for pulmonary tuberculosis or radiographs taken for insurance or immigration purposes,
(ii) that the principle *as low as reasonably practicable* (ALARA) must be applied at all times and non-radiation techniques used whenever appropriate and
(iii) that in the case of well-person screening for pre-clinical disease, the criteria for value must be critically examined, and the risks fully explained.

Possible effects of radiation include not only cancer induction, which is that most commonly mentioned, but also others, and may be grouped as follows:
(i) psychological, (ii) scarring and (iii) nuclear.
In each category the effects may be cumulative over repeated exposures, and differences exist between the possible effects of "localized" radiation and systematically administered radiation. The categories are not mutually exclusive.

Psychological effects

(i) There is widespread fear of the unknown about radiation, not helped by the lack of immediate sensation during exposure and the knowledge that harm may follow, nor by the attitude (and indeed ignorance) of many doctors.
(ii) "Knowledge" that late effects might occur may come, in addition to explanations by the doctors or other staff concerned, from other patients, possibly seen in hospital, or from the media giving information about nuclear warfare, nuclear industry, etc.
(iii) As no (detectable) adverse effect ever follows the great majority of radiodiagnostic procedures and benefit follows, adequate explanation should eliminate any associated problem. However, considerable doses are delivered in some modern fluoroscopic procedures and late effects have been detected after repeated exposures, *e.g.* in patients treated by pneumothorax for pulmonary tuberculosis, while there are also worries about repeated mammography. Furthermore, the recent Exeter radiotherapy experience of the delivery of higher than prescribed doses may lead to doubts about the effective control of diagnostic methods.
(iv) In some recent accidents, *e.g.* the fire at King's Cross underground station and the Zeebrugge ferry disaster, the concept of damages for psychological trauma has been introduced, and this is likely to feature in the aftermath of the Exeter incident.
(v) Adequate explanation of all proposed examinations is therefore essential, and may be expected to reduce concern.
(vi) Although the proportional variations in dose in common practice are much less in therapy than in diagnosis, potentially they are more important because of the much larger doses involved.

Scarring

(i) Ionizing radiation is an inflammatory agent, and can cause direct cell death. Mild inflammation, hyperaemia and oedema, which must always occur, will resolve spontaneously. More severe inflammation will proceed to scarring or fibrosis. Cell death is followed by leucocytosis and phagocytosis, and later, fibrosis.

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*Based on an invited presentation at Radiology '89 at Eastbourne in May, 1989.

(ii) There may be transitory or permanent impairment or loss of function, *e.g.* epilation, loss of sweating, reduction of the thickness of the skin, reduction of salivation, depression of liver function, etc., depending on the tissues affected and the dose received.

(iii) The endothelium of small vessels undergoes late fibrosis leading to ischaemia and/or telangiectasis and consequent scarring of the tissues supplied with blood by the vessels, possibly leading to delayed healing or late necrosis, especially after minimal trauma or infection. These effects are largely related to the nature of the blood supply to the particular tissue, and are most important in those with limited reserve, such as the spinal cord and the kidney, well recognized by radiotherapists as critical tissues.

These effects are non-stochastic, *i.e.* have a threshold, vary in degree and are dose dependent. In the majority of diagnostic procedures they are undetectable, while for most therapy procedures they occur to a greater or lesser extent, and treatment techniques are constructed to minimize the risk, compatible with effective treatment.

Nuclear changes

These are "all-or-nothing", or stochastic, *i.e.* they cannot be partial and they occur or do not occur in a particular cell. There is thought to be no threshold below which the effect does not occur at all. Their frequency, *i.e.* the number of cells affected, increases with dose, though there is no general agreement as to whether the association is arithmetic or geometric.

Many types of change in genes and chromosomes have been described. Some lead to cell death at the next cell division, others may be transmitted to daughter cells. Most are recessive.

The effect becomes apparent only at a subsequent cell division, and therefore is more likely to be seen in rapidly dividing tissues, *e.g.* haemopoietic tissue and epithelium of small bowel mucosa or skin. There is a latent period before any effect is seen, and so the association with radiation often depends on detailed epidemiological studies. Consequently, arguments about causation arise.

The sensitivity of tissues to these effects varies with the maturity of the person, being lower in early adulthood than in childhood or in older age. This is one reason for the "pregnancy rule" in radiodiagnosis, because fetal tissues in general are relatively sensitive.

The *detectable effect* of nuclear changes may be either the development of a cancer or of a fetal abnormality.

With very few exceptions, there are no definite features of a cancer which identify it as being radiation induced, distinct from cancers of the same tissue and type arising spontaneously or from the effects of other carcinogens. The effects of different carcinogens on a given tissue may be additive or synergistic. Therefore when any cancer develops the question of causation arises, though the majority appear "spontaneously".

Experience from radiotherapy patients, and persons exposed in nuclear warfare and the nuclear industry, indicates that the likelihood of cancer or a fetal abnormality rises with dose. With special reference to cancer, and by a process of extrapolation from the known effects of large doses to the possible effects of small doses, making the assumption that no threshold exists, the concept of a "doubling dose" results. This is a dose which doubles the population incidence of the particular cancer, and suggests that of the total number of cancers half may be attributed to radiation exposure. Therefore in a person who has received a doubling dose for the particular tumour it may be assumed in the legal sense that the tumour is radiation induced.

Occurrence

If and when "damage" occurs, the following steps are necessary to pursue a medicolegal action:

(i) The "damage" must be accurately diagnosed, anatomically and pathologically, and, now, possibly psychiatrically.

(ii) Proof of radiation exposure is needed, including an estimate of dose to the particular tissue (often very difficult in radiodiagnosis), and a knowledge of time lapse. The dose must be related to doses known to have caused the same type of lesion, *e.g.* fibrosis or epilation, or to the accepted doubling dose for a cancer. Similarly, the time interval must be appropriate, *e.g.* longer for some solid cancers (15–40 years according to site) than for leukaemia (usually between 5 and 15 years).

(iii) Other causes of the same lesion, *e.g.* other carcinogens or other causes of scarring, to which there has been exposure must be taken into account. The possibility of combined action by different causes must be considered, *e.g.* smoking in uranium mine-workers.

(iv) A level of proof must be established. The difference between a scientific level (usually more than 95%) and the legal level in civil cases, "on the balance of probabilities" (*i.e.* more than 50%), is often not appreciated by the medical profession.

(v) The statute of limitations requires that a case is opened within 3 years of the knowledge of an effect resulting from an exposure, except in the case of children. Knowledge usually dates from a diagnosis being made.

(vi) Negligence must be shown on the part of some agency, *e.g.* Health Authority or doctor. The most important measures relevant to such cases are the Health and Safety at Work etc. Act, 1974, the Ionising Radiation Regulations, 1985 and associated codes, and the Regulations for the Protection of the Patient, 1988 (proof of negligence is not necessary in the case of non-medical exposures in the Nuclear Industry, where evidence of dose delivered is sufficient, provided that the case is brought within 30 years of the exposure).

(vii) In defence, the "reasonableness" of the procedure involved should be supported by showing it to be the practice of "a body of similar colleagues", but not necessarily the whole of the profession. Advice such as that published from time to time by the Royal College of Radiologists and the medical defence organizations is helpful but not mandatory.

1990, *The British Journal of Radiology*, *63*, 315–317

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Final Report of the BIR fractionation study

THE EDITOR—SIR,

Wiernik et al (1990) have reported on the BIR multicentre trial of 3 *versus* 5 days per week treatment of tumours of the larynx and pyriform sinus. No statistically significant differences were found between the two arms with respect to survival and complication rates.

The purpose of choosing irradiation over surgery in the tumours of the laryngopharynx is to preserve the larynx. Salvage surgery is highly successful, primarily for failures in patients with mobile cord tumours, but it also has been successful in other sites where, in addition to laryngectomy, radical neck dissection can be curative. Therefore, survival rates do not reflect the effectiveness of the radiation treatment, yet survival analysis makes up the bulk of their report. The brief analysis of the incidence of laryngectomies is lost in an extensive text on statistical methods and a large number of tables and graphs relating to survival rates.

There are in this series two different types of tumours: (1) those of the mobile cords, which present rarely with palpable neck nodes, as substantiated in the present material, and (2) those of the supraglottic larynx and pyriform sinus. These two types of tumours must be analysed separately if one really wants to have a true picture of the effectiveness of 3 *versus* 5 days a week treatment. The endpoint for the mobile cords is a failure in the larynx. For the other sites, which present with a significant incidence of palpable neck nodes, the endpoints should be both incidence of failures at the primary site and failures in the neck.

A final point to keep in mind is that multicentre studies may not be meaningful (Tubiana et al, 1986). The present trial included a large number of centres with widely variable treatment techniques. This variability can confound interpretation of the results, as illustrated by an Intercontinental Study carried out to find the value of dissecting the internal mammary chain nodes in tumours of the breast. A preliminary analysis seemed to show improved survival rates by dissecting the chain in tumours of the inner quadrants with histologically positive nodes in the axilla (Lacour et al, 1976). The difference disappeared in a 10 year analysis for the multicentre trial, but was preserved with statistical significance in the group of patients treated at The Institut Gustave Roussy (Lacour et al, 1976, 1983). It is worrisome that a similar confounding effect may have influenced the BIR 3 *versus* 5 days per week trial: the overall times ranged from 3 to 6 weeks and the geometries in the treatment fields at the different centres were likely different.

For the reasons given, I believe that the Final Report of the BIR fractionation study of 3 *versus* 5 fractions per week is of little help to the clinician who must decide on the best dose/fractionation regime for patients with laryngeal cancer.

Yours, etc.,
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(*Authors' reply*)

THE EDITOR—SIR,

We were interested to see Dr Fletcher's comments on the Final Report of the BIR Fractionation Working Party's trial of 3F/wk *versus* 5F/wk in the treatment of carcinoma of the laryngo-pharynx. Any reader examining the report in detail will, we believe, find very little evidence to support Dr Fletcher's criticisms.

In the final analysis, what a patient is interested in is survival, so no apologies are needed for addressing the issue of overall survival in the first instance. However, Dr Fletcher's statement that "survival analysis makes up the bulk of their report" is quite unjustified. Equal weight has been given in the report to three parameters: (1) overall survival, (2) tumour-free rates and (3) laryngectomy-free rates. The effectiveness of radiation treatment is shown by success or failure at the primary site, and this is measured directly by the incidence of tumour persistence or later recurrence and the need for laryngectomy. While Figs 1 and 2 of the report show overall survival comparisons, Figs 3 to 6 compare the time course of tumour recurrences (including tumour persistence) and laryngectomies. In Table III, all three types of failure, death, tumour persistence or recurrence and laryngectomy, are given equal prominence. Where are the "large number of tables and graphs relating to survival rates" of which Dr Fletcher complains?

By suggesting that the Final Report is based on the two types of tumour, which he quotes, Dr Fletcher appears not only to mix up our primary tumour categories that had been carefully segregated according to the TNM classification but also to pick these arbitrarily from the 12 tumour categories that were actually specified on the entry form for use in the BIR fractionation trials. Dr Fletcher again seems to ignore the separate analyses of results in larynx and pharynx plus dual tumours presented in Table III of the report, and the comparisons for subsets of patients with mobile cords and by nodal status in Figs 4, 5 and 6. Although only recurrence at the primary site was used for the calculation of tumour-free rates, recurrence in the neck nodes *without* recurrence at the primary site was very rarely observed in these patients.

The pros and cons of multicentre trials have been widely argued in the literature and we do not consider these correspondence columns to be the proper place to add to those arguments. The particular point raised by Dr Fletcher about the possible confounding effect of different overall treatment times was examined by the Working Party and is reported in the tumour control section of the Discussion. No such effect was apparent.

Finally, Dr Fletcher chooses to dismiss the report as being "of little help to the clinician who must decide on the best dose/fractionation regime for patients with laryngeal cancer". In the first place, the BIR Fractionation Working Party has never claimed to address the problems associated with dose/fraction in a given regime as the dose/fraction differed in each of the participating centres; the trial asked a quite different question, namely, was treatment given in 3 fractions per week as good for the patient as treatment given in 5 fractions per week. Secondly, besides the tabulated information on 3, 5 and 10 year rates, together with their associated errors, the report also includes estimated values of relative risks of death, recurrence and laryngectomy and their 95% confidence intervals. These provide hard data for a clinician who has to weigh the obvious socio-economic benefits of using a reduced number of fractions against any potential therapeutic risk that might exist. We can only express our surprise that Dr Fletcher should dismiss such data as unhelpful.

Yours, etc.,
GEORGE WIERNIK (CHAIRMAN)
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References

LACOUR, J., BUCALOSSI, P., CACERES, E., JACOBELLI, G., KOSZAROWSKI, T., LE M., RUMEAU-ROUQUETTE, C. & VERONESI, U. 1976. Radical mastectomy versus radical mastectomy plus internal mammary dissection: five-year results of an international cooperative study. *Cancer, 37*, 206–214.

LACOUR, J., LE M., CACERES, E., KOSZAROWSKI, T., VERONESI, U. & HILL, C., 1983. Radical mastectomy versus radical mastectomy plus internal mammary dissection. Ten-year results of an international cooperative trial in breast cancer. *Cancer, 51*, 1941–1943.

TUBIANA, M., ARRIAGADA, R. & SARRAZIN, D., 1986. Human cancer natural history, radiation induced immunodepression and post-operative radiation therapy. *International Journal of Radiation Oncology, Biology, Physics, 12*, 477–485.

WIERNIK, G., BATES, T., BLEEHEN, N., BRINDLE, J., BULLIMORE, J., FOWLER, J., HAYBITTLE, J., HOWARD, N., LAING, A., LINDUP, R., MCGIURK, F., PHILLIPS, D. & REZVANI, M., 1990. Final report of the general clinical results of the British Institute of Radiology fractionation study of 3F/week *versus* 5F/week in radiotherapy of carcinoma of the laryngo-pharynx. *British Journal of Radiology, 63*, 190–201.

Sedation for CT examinations in children

THE EDITOR–SIR,

A few years ago I made extensive enquiries as to the most effective sedation for computed tomographic (CT) examinations in children under 4 years of age. The answers were diverse. In the USA intra-muscular Nembutal was commonly used, in Europe various cardiac cocktails were popular, whilst others preferred a light general anaesthetic. On a trip to Australia last year, I noted that at least three major paediatric centres used a general anaesthetic. This delayed the procedures and reduced the numbers of possible CT examinations to a maximum of half-a-dozen a day.

For the last 2 years we have used simple chloral hydrate, and not only is it 98% effective, but it enables us to perform between 12 and 18 CT examinations in a routine day.

It is given in the form of a palatable syrup in the dosage of 75–100 mg per kilo (Foulner, 1990). It is dispensed as 60 mg per ml so that a 2-year-old, 12 kg child would receive about 15–20 ml. This is usually administered by a syringe into the mouth, but in very uncooperative children a nasogastric tube is used. The only time we have not found this effective is in mentally retarded children.

This form of sedation is effective and safe with the following caveats:

(1) A serene and confident ambience is required. The dose is administered in an ante-room and the children have toys to play with. They are reassured by their parents' presence, who also accompany them into the CT room. It is usually only 30–40 min before they fall into a natural sleep and can be gently immobilized for the examination.

(2) When an intravenous injection of contrast medium is likely to be required, then an intravenous line must be placed *in situ* before the child is placed on the CT table. This should be thought about beforehand, as children become fractious when woken from sleep for injection.

(3) Fast scanning speeds of 2 s or under are preferred, but not totally essential, requirements.

This is a simple regime that works, However, good CT in the young does not come by accident, and details about bowel and intravenous contrast media should be worked out before a child is sedated.

Yours, etc.,
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(*Received July 1989*)

Reference

FOULNER, D., 1990. A sweet solution to a contrast problem. *British Journal of Radiology, 63*, 219–220.

The influence of tube type and operator experience on performance of small bowel enema

THE EDITOR–SIR,

Recent correspondence (Bisset, 1989) concerning the techniques and different types of nasogastric tubes mentions the re-use of tubes after sterilization. A problem common to many tubes is manipulating the guidewire once the tube has become slightly softened by chemical sterilization. Silicon gel is used routinely during endoscopy to facilitate catheter or guidewire insertion through the instrument. Only a few ml is required, either injected into the tube, or with the guidewire simply dipped into the gel prior to insertion. This will overcome any problem inserting, turning or withdrawing the guidewire, and is an inexpensive way to prevent any difficulty manipulating guide wires when catheters are re-used. I would recommend this as a standard manouvre for the cost conscious.

Yours, etc.,
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(*Received November 1989*)

Reference

BISSET, R., 1989. The influence of tube type and operator experience on performance of small bowel enema. *British Journal of Radiology, 62*, 953–954.

Alterations in body and skin temperatures caused by MRI

The Editor–Sir,

The recent paper by Shellock et al (1989), which describes skin and body temperatures and cutaneous blood flow in six volunteers before, during and after magnetic resonance imaging (MRI) procedures performed at high specific energy absorption rates (SARs), is critical of some aspects of the NRPB recommendations (NRPB, 1983) for limiting patient (and volunteer) exposure to radiofrequency (RF) magnetic fields during MRI. The paper, and other recent papers by these authors, are a welcome addition to our knowledge of the effects of RF absorption in the human body, which was rather more limited when NRPB formulated its recommendations. The points made by Shellock et al that limits of 0.4 W/kg on the mean specific energy-absorption rate (SAR) and of a 1°C rise in temperature shown by the skin are too conservative are well taken, as is also their point that measurement of temperature in the sublingual pocket might be preferable to measurement in the rectum. These points will be addressed in revised NRPB advice in regard to magnetic resonance imaging which is being prepared.

Shellock et al (1989) also draw attention to two further important points relevant to limits on RF exposure during MRI: that additional studies should be performed to determine the possible presence of deep tissue heating, and that the response to high SARs of patients with impaired thermoregulatory function should be assessed. Present uncertainty about these considerations is bound to impose some constraints on any proposed relaxation of limits of RF exposure based on the whole-body response of healthy volunteers.

The limit of 0.4 W/kg^{-1} is also used in guidance on restrictions on occupational and public exposures to radiofrequency and microwave radiation (INIRC, 1988; NRPB, 1989). The point must be made that exposures in these contexts may be for prolonged periods. It is relevant therefore that the data of Shellock et al show that at a mean SAR of 2.8 W/kg in a healthy subject the skin temperatures on the abdomen and forearm were still increasing after about 30 min of exposure with no sign that an equilibrium temperature had been reached. Moreover, in their exposure conditions, the main heating from the RF field was in the outer layers of the body; this might not be the case for other types of exposure. If anything, therefore, for prolonged occupational or public exposures, 0.4 W/kg might not be too far from a tolerable limit for persons with impaired thermoregulation in adverse environmental conditions.

Yours, etc.,
J. A. Dennis
R. D. Saunders

National Radiological Protection Board,
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(*Received November 1989*)

(*Authors' reply*)

The Editor—Sir,

Thank you for allowing us to respond to the letter from J. A. Dennis and R. D. Saunders concerning our recent article (Shellock et al, 1989).

We would like to indicate that the United States Food and Drug Administration (FDA) has relaxed the guidelines for exposure to radiofrequency (RF) electromagnetic fields during clinical magnetic resonance imaging (MRI) based, in part, on our recent publications as well as those from other investigators.

The newly recommended acceptable exposure levels for RF radiation during MRI are as follows:

(a) a whole-body averaged specific absorption rate (SAR) of $\leqslant 0.4$ W/kg, spatial peak in 1 g of tissue of $\leqslant 8.0$ W/kg, and 3.2 W/kg averaged over the head *or*, alternatively,

(b) those that do not cause a body core temperature >1°C, except for patients with impaired systemic blood flow or perspiration (*i.e.* patients with compromised thermoregulatory systems), local exposures of <38°C in the head, <39°C in the trunk, and <40°C in the extremities. The above exposure levels apply to normal clinical environments where the individual is resting and lightly dressed.

We would like to point out that the FDA has allowed certain manufacturers and their users to perform clinical MRI at whole-body averaged SARs up to 4.0 W/kg, since their safety documentation and data demonstrate that the above *temperature* criteria are not exceeded even at these SAR levels.

We regard this to be especially important because it is obvious that there is not a good relationship between SARs and temperature changes, particularly in patient populations (Shellock & Crues, 1987) and, therefore, an indication of temperature criteria is necessary for useful and pertinent MRI safety guidelines for RF radiation.

We hope that the NRPB considers the above while revising the safety recommendations for MRI.

Yours, etc.,
Frank G. Shellock
*Daniel J. Schaefer
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(*Received December 1989*)

References

INIRC, 1988. Guidelines on limits of exposure to radiofrequency electromagnetic fields in the frequency range 100 kHz to 300 GHz. *Health Physics*, *54*, 115–123.

NRPB, 1989. Guidance as to restrictions on exposures to time varying electromagnetic fields and the 1988 recommendations of the International Non-Ionising Radiation Committee. *National Radiological Protection Board Guidance on Standards, NRPB-GS11.*

Shellock, F. G. & Crues, J. V., 1987. Temperature, heart rate, and blood pressure changes associated with clinical MR imaging at 1.5 T. *Radiology*, *163*, 259–262.

Shellock, F. G., Schaefer, D. J. & Crues, J. V., 1989. Alterations in body and skin temperatures caused by magnetic resonance imaging: is the recommended exposure for radiofrequency radiation too conservative? *British Journal of Radiology*, *62*, 904–909.

1990, *The British Journal of Radiology*, *63*, 318–323

Proceedings of The British Institute of Radiology

Imaging in abdominal sepsis

Abstracts of papers presented at a meeting of the BIR held at 36 Portland Place, London W1N 4AT, on Thursday, 19 October 1989

Chairman: Professor G. M. Roberts

Intra-abdominal abscess: the role of the plain radiograph, by Dr M. Creagh
Ultrasound—the beginning or the end? by A. E. A. Joseph. Abstract not received
Radionuclide imaging and abdominal sepsis, by M. Peters. Abstract not received
Diagnostic aspiration and therapeutic drainage using CT, by S. Golding

Intra-abdominal abscess: the role of the plain radiograph

Dr M. Creagh
Department of Radiology, St Thomas' Hospital, London

The plain abdominal radiograph is often the first investigation a patient experiences following clinical evaluation. Contrary to popular belief, patients with intra-abdominal abscesses are not always critically ill, and as the radiological signs of intra-abdominal abscess are often subtle the radiologist must play a key role in the diagnosis. Of critical importance is a thorough understanding of the peritoneal reflections within the abdomen. Paradoxically these peritoneal reflections constitute both barriers and conduits, impeding and facilitating the passage of intra-peritoneal effusions. Abscesses may range in size and may cause considerable mass effect. Gas within an abscess is very helpful from the point of view of plain radiograph evaluation, and may vary in appearance from tiny lucencies within soft tissue density material to a single collection outlining the oedematous, irregular wall of an abscess cavity. Where initial plain radiographs are equivocal, further radiographic techniques should be employed. The use of horizontal beam, lateral and decubitus views together with gastrointestinal contrast media studies may be sufficient to confirm suspicions engendered by the initial plain radiograph findings. The importance of serial films indicating enlarging or fixed collections of gas is emphasized. There are, in addition to the specific plain radiograph findings mentioned above, a multitude of plain radiograph abnormalities which, although not diagnostic of sepsis, may raise suspicions as to the presence of infection, both loculated and diffuse. Examples include free intraperitoneal gas, gas within the wall of a viscus, biliary/urinary tract gas and portal venous gas. Unusual calcifications such as those seen in appendicoliths are important. Ileus and loss of normal fat planes are not to be underestimated, and finally, a chest radiograph can be of value in providing clues to pathology below the diaphragm.

Diagnostic aspiration and therapeutic drainage using CT

Stephen J. Golding
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The objective of treating abdominal sepsis is to find and drain pus at the earliest opportunity. Patients may be suffering from toxaemia or septicaemia, recovering from a major surgical procedure or otherwise critically ill, making them poor candidates for surgical drainage. However, the less invasive alternative of percutaneous drainage needs to be effective if it is not to delay definitive treatment. Both computed tomography (CT) and ultrasound are accurate methods of detecting abdominal fluid collections (Knochel et al, 1980; Mueller & Simeone, 1983). Computed tomography has the advantage that it is not impeded by bowel gas and it is more useful than ultrasound in the central abdomen. However, ultrasound is readily available, can be taken to the patient if the patient is too sick to move, and is very accurate in the upper abdomen and around the bladder; it may therefore be employed first and CT reserved for difficult cases (Mintz et al, 1983; Joseph, 1985). They share the disadvantage that it may not be possible to distinguish abscesses from other fluid collections and diagnostic aspiration may be needed. Percutaneous aspiration may be used to confirm the presence of pus and to obtain a specimen for culture but the aim of treatment should be to evacuate the cavity completely, and most patients need to proceed to a drainage procedure. This may be achieved either by manual aspiration as a single procedure or by the insertion of an indwelling catheter. While both ultrasound and CT may be used for siting needles for diagnostic aspiration, the more precise anatomical information provided by CT is invaluable for placing drainage catheters, particularly in relation to bowel loops (vanSonnenberg et al, 1982; Clark & Towbin, 1983). Whichever technique is used, percutaneous abscess drainage may be expected to be safe and successful in nearly all patients (Martin et al, 1984). The effect on the clinical state of the patient is often dramatic and, even where complete drainage fails, the patient's condition may be improved sufficiently for surgical drainage to be carried out at less risk, or less extensively (Lang et al, 1986; Mueller et al, 1987). In my opinion, surgical drainage of abscesses should now not be undertaken until percutaneous drainage has been considered or has been tried and failed. Furthermore, the availability of this technique means that radiological management of these problems may now be based on patho-physiological principles and conventional procedures which interfere with resolving abscess cavities, such as sinography, may no longer be appropriate in the majority of patients.

References

Clark, R. A. & Towbin, R., 1983. Abscess drainage with CT and ultrasound guidance. *Radiologic Clinics of North America, 21*, 445–459.

Joseph, A. E. A., 1985. Imaging of abdominal abscesses. *British Medical Journal, 291*, 1446–1447.

Knochel, J. Q., Koehler, P. R., Lee T. G. & Welch, D. M., 1980. Diagnosis of abdominal abscesses with computed tomography, ultrasound and ^{111}In leukocyte scans. *Radiology, 137*, 425–432.

Lang, E. K., Springer, R. M., Glosiroso, L. W. & Cammarata, C. A., 1986. Abdominal abscess drainage under radiologic guidance: cause of failure. *Radiology, 159,* 329–336.

Martin, E. C., Fankuchen, E. I. & Neff, R. A., 1984. Percutaneous drainage of abscesses: a report of 100 patients. *Clinical Radiology, 35,* 9–11.

Mintz, M. C., Arger, P. H. & Kressel, H. Y., 1983. An algorithmic approach to the radiologic evaluation of a suspected abdominal abscess. *Seminars In Ultrasound, 4,* 80–90.

Mueller, P. R. & Simeone, J. F., 1983. Intraabdominal abscesses: diagnosis by sonography and computed tomography. *Radiologic Clinics of North America, 21,* 425–443.

Mueller P. R., Saini, S., Witterburg, J., Simeone, J., Hahn, P. F., Steiner, E., Dawson, S. L., Butch, R. J., Stark, D. D., Ottinger, L. W., Radkey, G. V., Bousquet, J.-C. & Ferrucci, jr, J. T., 1987. Sigmoid diverticular abscesses: percutaneous drainage as an adjunct to surgical resection in 24 cases. *Radiology, 164,* 321–325.

vanSonnenberg, E., Ferrucci jr, J. T., Mueller P. R., Wittenberg J. & Simeone, J. F., 1982. Percutaneous drainage of abscesses and fluid collections: technique, results and applications. *Radiology, 142,* 1–10.

Vascular effects in tumour therapy

Abstracts of papers presented at an all-day meeting of the BIR held at the British Institute of Radiology on Friday, 10 November, 1989

Chairman: Dr I. J. Stratford

Aspects of antivascular tumour therapy, exemplified by photodynamic therapy, by J. V. Moore
The effect of flavone acetic acid on coagulation and permeability in experimental tumours, by G. Thurston, A. Smith and C. Murray
Induction of endothelial cell procoagulant activity by flavone acetic acid is potentiated by a tumour-derived mediator, by C. Murray, G. Thurston and D. Stern
The effect of fractionated radiotherapy on the uptake of ^{3}H-Vincristine by a mouse carcinoma, by G. D. Zanelli, L. Rota and M. Trovo
The effect of tumour necrosis factor on experimental tumours—induction of hypoxia and interaction with bioreductive drugs, by H. S. Edwards, J. C. M. Bremner and I. J. Stratford
The vasodynamics of mouse tumours, by A. H. W. Nias and P. M. Perry
Vascular changes in experimental tumours monitored by ^{31}P NMR, by P. Wood, J. Bremner, C. Counsell and G. Adams
Modification of the blood flow and the energy metabolism of transplanted rat tumours using antihypertensive agents, by G. M. Tozer, R. J. Maxwell, J. R. Griffiths, E. Proctor and A. Busza
Variation in normal-tissue vascular response to agents that modify tumour blood flow, by D. J. Honess
Differences in the response of the vasculature in primary and transplanted tumours, by S. B. Field, I. A. Burney, S. Needham, J. E. Maxwell and J. R. Griffiths
Neovasculature as a novel target in tumour therapy, by J. Denekamp

Aspects of antivascular tumour therapy, exemplified by photodynamic therapy

J. V. Moore
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In photodynamic therapy, two agents that are in themselves non-toxic: porphyrins, or related compounds, and visible light, in combination produce locally-cytotoxic moieties such as singlet molecular oxygen. *In vitro*, isolated tumour cells and three-dimensional spheroids are directly destroyed by photodynamic therapy (PDT) but following systemic injection *in vivo*, there is increasing evidence that tumour destruction is mediated by vascular injury. The literature of PDT now contains several examples of prompt (within minutes) damage to endothelium evidenced by electron and light microscopy. *In vitro* comparisons with tumour and normal-tissue lines suggest that endothelial cultures are among the most sensitive to the effects of PDT. This damage to the endothelium is enhanced if the cells are in log rather than plateau phase, which may indicate the possibility of a therapeutic advantage between tumours and normal tissues. Injury to endothelial cells leads to the release of clotting factors which contribute to the characteristic vessel occlusion seen after PDT. Such vessel occlusion results in the rapid, secondary death of large numbers of dependent tumour parenchymal cells, the extent of the injury being a function of drug and light doses. This massive coagulative necrosis may be readily imaged by magnetic resonance and is predictive for therapeutic outcome. Reasons for failure using this vascular-mediated therapy are discussed, together with the nature of possible adjuvant therapies.

The effect of flavone acetic acid on coagulation and permeability in experimental tumours

G. Thurston, A. Smith and C. Murray
CRC Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex

Flavone acetic acid (FAA) is an anti-tumour drug that is effective against a wide variety of experimental murine tumours. It is relatively non-toxic *in vitro*, it induces rapid haemorrhagic necrosis in tumours and is selectively effective against solid tumours, indicating an indirect action. We have examined the rapid effects (within 6 h) of FAA on coagulation and vascular permeability in mice, and found significant differences in the effect of FAA on tumour-bearing versus non tumour-bearing mice. In terms of coagulation, FAA induced an increase in the coagulation potential of plasma shortly after intraperitoneal administration (within 30 min in both tumour-bearing and non tumour-bearing mice). Only in tumour-bearing mice was this followed (at 4 to 6 h post-administration) by evidence of intravascular coagulation, including the presence of fibrin degradation products, depletion of platelets, and depletion of coagulation proteins. Experiments with anticoagulants, *e.g.* heparin or ancrod, showed little inhibition of the anti-tumour action of FAA or of the FAA-induced consumption of platelets. The effect of FAA on tissue permeability of various organs and tumours was measured in mice using radiolabelled albumin. There was no difference in the leakage of albumin after FAA in any of the tested organs in non tumour-bearing animals, nor in the kidney, fat pad, heart or spleen of tumour-bearing mice. However, the liver and tumour showed a dose-dependent increase in leakage at 2–4 hours after FAA, which correlates with the time of histologically evident damage in these tissues. These findings emphasize the unique characteristics of tumour vasculature and its potential role in the action of anti-tumour agents.

Induction of endothelial cell procoagulant activity by flavone acetic acid is potentiated by a tumour-derived mediator

Cliff Murray, Gavin Thurston and *David Stern

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Flavone acetic acid (FAA) induces a coagulopathy in mice which, in tumour-bearing animals, has many characteristics of an intravascular coagulation (Murray et al, 1990). This probably results from the activation of the "extrinsic" pathway of coagulation, which is mediated through the expression of tissue factor (TF) on the endothelial cell surface. This observation led us to examine whether the endothelium could be a cellular target for FAA, with a resultant modulation of cell surface coagulant properties leading to activation of coagulation and subsequent vascular occlusion. Confluent cultures of human umbilical vein endothelial cells (HUVEC) were pre-incubated for varying times with a range of FAA concentrations. After washing with fresh medium, clotting times of normal citrated human plasma were measured by incubating the plasma in direct contact with the cell monolayer. By comparison with a standard curve, clotting times were converted to TF equivalents. The results indicated that FAA increased the functional expression of TF in a time- and dose-dependent manner. The clot-promoting activity induced by FAA could be inhibited by cycloheximide and by preincubation of cells with a monoclonal antibody to TF. To explain the apparent selectivity of the action of FAA for tumour vasculature, we considered its interaction with tumour-derived mediators. Co-incubation of HUVEC with FAA and conditioned medium from a human melanoma cell line, FO-1, led to a 6-fold increase in tissue factor induction. By sequential ultrafiltration, ion-exchange and reverse phase chromatography, followed by preparative gel electrophoresis, we isolated a protease-sensitive factor (~20–25 000 mw) which not only promoted procoagulant activity in HUVEC, but strongly potentiated the activity of FAA, the combination producing a 27-fold increase in procoagulant activity. We hypothesize that FAA exerts its action, at least in part, by promoting direct activation of coagulation on the endothelial cell surface, and that this effect is selective for the tumour vascular bed by virtue of its interaction with a tumour-derived factor.

Reference

MURRAY, C. et al, 1990. *British Journal of Cancer*, in press.

The effect of fractionated radiotherapy on the uptake of ^{3}H-Vincristine by a mouse carcinoma

G. D. Zanelli, L. Rota and M. Trovo

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The uptake of ^{3}H-Vincristine in a transplanted mouse carcinoma (carcinoma NT in CBA mice) during a realistic course of radiotherapy has been investigated. Twenty-five fractions of 2 Gy each of Cobalt 60 radiation were given to the tumour 5 days a week for 5 weeks. Subgroups of tumour-bearing mice were withdrawn from the experiment each day and injected with 195 KBq of ^{3}H-Vincristine. The mice were killed 1 h later, the tumours and several normal tissues removed and their content of ^{3}H determined. The quantity of ^{3}H-Vincristine per g of tumour varies considerably during the course of radiotherapy. The variation is sinusoidal in character with peaks immediately after the weekend rest period and troughs in the middle of the week. The uptake per g of tumour at the peaks was more than three times that of non-irradiated tumours while at the troughs it fell to near zero. It is well known that radiation has profound effects on blood flow and capillary permeability in both normal and malignant tissues and that these effects are dependent on the radiation dose and the time after irradiation. The elucidation of this time-dose relationship may be useful in the planning of combined modality treatment (CMT) involving radiotherapy and chemotherapy.

The effect of tumour necrosis factor on experimental tumours—induction of hypoxia and interaction with bioreductive drugs

H. S. Edwards, J. C. M. Bremner and I. J. Stratford

MRC Radiobiology Unit, Chilton, Didcot, Oxon

Viable hypoxic cells exist in the regions of tumours between the well oxygenated cells and the dead necrotic regions. Such cells are radiation-resistant and may limit the response of a tumour to radiotherapy. However, hypoxic cells are also selectively killed by bioreductive drugs which are bioactivated under conditions of hypoxia. It is possible to reduce the supply of oxygen (and other nutrients) to tumour cells by decreasing the tumour blood flow. This may result in an increase in the proportion of hypoxic cells. Such effects may be exploited by combination with bioreductive drug therapy. Physical clamping occludes the blood supply to tumours thus decreasing the supply of oxygen. This is known to produce nearly 100% radiobiological hypoxia. Tumour necrosis factor (TNF) modulates the activity of certain immune system components leading ultimately to a reduction in tumour blood flow. We studied how TNF treatment influences the radiobiological hypoxic fraction using an *in vivo/in vitro* clonogenic assay. The radioprotective effect of clamping was compared to that produced by various concentrations of TNF administered to mice at various times prior to irradiation. When TNF was given at a dose of 2.5×10^{5} U/Kg an increase in tumour hypoxia was seen after 30 min. Almost 100% radiobiological hypoxia (equivalent to that resulting from clamping) was reached by 1 h after treatment, and lasted for up to 16 h. The minimum dose of TNF that produced a level of hypoxia comparable to clamping was 1×10^5 U/Kg when administered 3 h prior to irradiation. We went on to combine TNF with the bioreductive drug RSU 1069 in both the KHT and RIF-1 murine sarcomas. The enhancement of bioreductive drug toxicity was measured in a regrowth delay assay. When an 80 mg/kg dose of RSU 1069 was administered 3 h after TNF (1×10^5 U/kg), no significant growth delay was seen. Another agent, flavone acetic acid (FAA), has been shown to produce nearly 100% radiobiological hypoxia this effect being mediated by a similar anti-tumour activity to TNF. A combination of FAA (200 mg/kg) given 2 h before an 80 mg/kg dose of RSU 1069 resulted in mean specific growth delays of 3.1 ± 0.6 in the KHT sarcoma and 3.6 ± 1.0 in the RIF-1 sarcoma. A second bioreductive drug SR 4233 was combined with the same FAA treatment and produced specific growth delays of 6.5 ± 1.1 and 3.7 ± 0.4 in the KHT and RIF-1 tumours respectively. Both RSU 1069 and SR 4233 alone have no effect on tumour growth. When TNF and FAA were given alone, growth delays of 0.51 ± 0.3 and 3.3 ± 0.7, respectively, were seen. In conclusion, the potentiation of RSU 1069 activity was greater in combination with FAA than with TNF. Flavone acetic acid enhanced the bioreductive toxicity of the maximum tolerated dose of SR 4233 more than that of the maximum tolerated dose of RSU 1069. We are currently investigating the anti-tumour effectiveness of TNF and SR 4233 in combination.

The vasodynamics of mouse tumours

A. H. W. Nias and P. M. Perry

Richard Dimbleby Department of Cancer Research, UMDS, St Thomas' Hospital, London

As part of our study of the oxygen effect on the radiosensitivity of C_3H mouse mammary tumours, our group has used oxygen polarography, ^{133}Xenon clearance, ^{86}Rubidium extraction and ^{31}P nuclear magnetic resonance (NMR) spectroscopy of the tumours in mice breathing oxygen at various partial pressures with and without anaesthesia. One effect of ketamine and diazepam anaesthesia is that the oxygen consumption of tumour cells is reduced by half. Since the blood supply to the tumour is maintained, however, the net effect is a reduction in the hypoxic fraction and a consequent increase in the radiosensitivity of such tumours. The time interval between anaesthesia and irradiation is important. If tumours are irradiated only 10 min after the induction of anaesthesia the radiation response is reduced. If they are irradiated after 40 min there is an increase in radiosensitivity, particularly in mice breathing oxygen. The NMR spectroscopy showed a reduction in the B-ATP peak at 10 min, but an increase at 40 min. This seems to indicate that anaesthesia induces a reversible pattern in the oxygen and glucose supply to the tumour, probably as a consequence of initial vasoconstriction and subsequent vasodilation of the tumour blood vessels. This pattern could be exploited in tumour therapy.

Vascular changes in experimental tumours monitored by ^{31}P NMR

P. Wood, J. Bremner, C. Counsell and G. Adams

MRC Radiobiology Unit, Chilton, Didcot, Oxon

Tumour oxygenation may be manipulated by altering tumour or host physiology in order to enhance the effectiveness of anti-cancer therapies. The vasodilator hydralazine is an agent which increases radiobiological hypoxia in tumours. Increased tumour oxygenation and radiosensitivity can be induced by the calcium antagonist, flunarizine, and by nicotinamide. The technique of *in vivo* ^{31}P nuclear magnetic resonance (NMR) spectroscopy has provided a means for more detailed study of some aspects of the metabolic response of tumours to oxygen manipulation. In the present study, hydralazine, flunarizine and nicotinamide have been examined for their ability to alter the *in vivo* ^{31}P spectrum in a number of experimental mouse tumours. All tumours were implanted intradermally on the back of the mouse, 2 cm from the base of the tail; KHT, SCCVII and RIF-1 tumours were implanted in C3H mice, and KHT and HX118 were implanted in nu/nu mice. Spectra were obtained using a 4.7 T 30 cm bore horizontal magnet, interfaced with a SISCO 200 spectrometer. A 7 mm diameter surface coil was used over the tumour, and 256 scans, with a delay of 2 s, were collected for each spectrum. Preliminary results using anaesthetized mice indicate that 5 mg/kg i.v. hydralazine reduces the normal temperature and pressure peaks to background, with a large rise in P_i, for up to 24 h after injection, in KHT and RIF-1 tumours in C3H mice. In unanaesthetized mice, the spectra returned to normal 3 h after injection. Hydralazine produced no change in the ^{31}P spectrum from HX118 tumours, with an intermediate response in the KHT tumours implanted in nu/nu mice. Flunarizine at 5 mg/kg i.p. and nicotinamide at 1000 mg/kg i.p. both reduce the P_i peak in SCCVII tumours by about 50% in unanaesthetized mice. The optimal times for this reduction coincide with those for maximal radiosensitization. These results suggest that ^{31}P NMR spectroscopy may provide valuable information about the metabolic responses to manipulation of tumour perfusion, in addition to that from other experimental endpoints.

Modification of the blood flow and the energy metabolism of transplanted rat tumours using antihypertensive agents

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Drug-induced selective reduction in tumour blood flow and secondary induction of tumour hypoxia and lowered tumour pH have potential for improving the efficacy of various forms of therapy. The effect of two vasodilators, hydralazine and prostacyclin, on blood flow, energy metabolism and pH of a transplanted rat fibrosarcoma, were studied using hydrogen washout and ^{31}P magnetic resonance spectroscopy (^{31}P MRS). The results were compared with the effects of blood loss on these parameters. The aims of the study were (1) to find out how large a reduction in systemic blood pressure is required in order to produce changes in tumour blood flow, energy metabolism and pH and (2) to investigate the relationship between primary changes in blood flow and secondary changes in energy metabolism and pH. A linear relationship was observed between drug-induced reduction in mean arterial blood pressure (MABP) and reduction in tumour blood flow. Hydralazine and prostacyclin produced the same fall in blood flow for the same reduction in MABP. Blood loss was slightly less effective for the same fall in blood pressure. Changes in ^{31}P spectra were only apparent when drug doses were sufficient to reduce MABP below around 65 mm Hg. Nucleotide triphosphates (NTP) and phosphocreatine (PCr) were then found to decrease and inorganic phosphate (P_i) increase; pH also decreased. However, the magnitude of these changes was much greater for hydralazine than for prostacyclin. This is thought to be because of a direct effect of hydralazine on tumour energy metabolism. Comparison of measurements of blood flow and phosphate metabolites showed that nutrient deprivation began to occur when blood flow through the tumour was reduced to around 20 mls 100 g^{-1} min^{-1}. Blood loss resulted in a significant reduction in tumour pH comparable to that induced by the vasodilators. However, phosphate metabolites remained unaffected. It is speculated that catecholamine release due to blood loss would increase anaerobic glycolysis in the tumour thus maintaining levels of high energy phosphates whilst decreasing pH. In conclusion, relatively low doses of hydralazine and prostacyclin were effective in reducing tumour blood flow and the degree of reduction was directly related to fall in MABP. However, these drugs are likely to be ineffective in altering tumour energy metabolism clinically because of the severe systemic hypotension involved.

Variation in normal-tissue vascular response to agents that modify tumour blood flow

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Agents that can selectively modify tumour blood flow or oxygenation status have broad potential applications in cancer therapy. Selective reduction of tumour blood flow may be exploitable to potentiate chemotherapy (especially bioreductive drugs), hyperthermia and thermochemotherapy. In mice, the vasodilator hydralazine (HDZ) at 5 mg/kg, and the haemoglobin modifier BW12C (Wellcome) at 70 mg/kg, can increase tumour hypoxia and decrease tumour blood flow. Nicotinamide (NCT) at 1000 mg/kg can radiosensitize some tumours, possibly by increasing blood flow. All three drugs are potential modifiers of both tumour thermosensitivity and chemosensitivity. The aim of the study was to investigate the time course of the effects of these agents on relative tissue perfusion (RTP) in normal tissues. The RTP was assayed by ^{86}Rb extraction (5–10 μCi per mouse 1 min before killing) on a variety of tumours and normal tissues in C3H mice. The following data, obtained 1 h after administration of the blood flow modifier, illustrate the findings:

	^{86}Rb extraction (RTP) as % of control		
Tissue	HDZ	BW12C	NCT
RIF-1 leg tumour 400 mm^3	32^a	65^a	94
RIF-1 flank tumour 400 mm^3	9^a	38^a	108
Leg muscle	105	88	73^a
Kidney	75^a	124^a	134^a
Liver	75^a	92	151^a
Lung	122^a	119^a	106

[a] Value different from 100% ($p<0.05$).

The RIF-1 tumour RTP is minimally perturbed by NCT, but reduced by BW12C and more so by HDZ, and the changes are size- and site-dependent. The agents have varying effects on the normal tissues assayed, *e.g.* RTP of the kidney is decreased by HDZ but increased by BW12C and NCT, but RTP of the liver is reduced by HDZ, unchanged by BW12C and increased by NCT. This suggests that these agents will probably have differing effects on the pharmacokinetics and normal-tissue toxicity of any co-administered chemotherapy. We conclude that tissue perfusion modifiers for combination with chemotherapy should be selected in the light of normal-tissue effects.

Differences in the response of the vasculature in primary and transplanted tumours

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The vast majority of studies on tumour vasculature use transplanted rodent tumours. However, their vasculature may be different from that of primary or spontaneous tumours. The purpose of this study was to test whether the vascular response, following perturbation, was similar in primary tumours to that in transplanted tumours derived from them. The perturbation used was a single intraperitoneal injection of 5 mg/kg hydralazine, which is known to cause hypoxia in transplanted tumours. Changes in perfusion were indicated by ^{31}P magnetic resonance spectroscopy (MRS) parameters $P_i/\Sigma P$ and $\beta NTP/P_i$. Ten primary skin tumours induced by irradiation given about 2 years previously were studied. Of these, only four showed a response to hydralazine, six did not. One of the non-responders was subsequently transplanted into isogenic recipient mice. Fourteen of the first, second and third generation transplanted tumours which arose were studied by MRS. Of these, 13 responded to hydralazine and only one did not. The difference is statistically significant ($p<0.01$). The histology of the transplanted tumours was similar to that of the primary. It is therefore clear that for the endpoint studied the transplanted tumours responded generally differently from the primaries. The reasons for the difference are not clear at this stage, although a number of possibilities have been examined, including the degree of malignancy, the volume of tumour at study, the latent period between derivation and experiment and the growth rate. A larger study will be needed to clarify the cause of the difference. One important conclusion from this study is that transplanted tumours may not always provide a suitable model for tumour vasculature.

Neovasculature as a novel target in tumour therapy

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The poor structure of tumour vasculature has been recognized for decades, mainly because the inadequate supply of oxygen gives rise to radioresistance in hypoxic cells. Much effort in radiobiology has focused on methods of overcoming this radioresistance. Until recently these hypoxic cells have been unstainable, but were considered to be those at the boundary of the cuff of viable cells around each vessel, adjacent to necrosis. Recent developments with bioreductive agents have made it possible to visualize these cells using radioactive tracers or immunohistochemistry. Approximately one decade ago, the thermosensitivity of the hypoxic cells resulting from acidity, nutrient deficiency and poor heat dissipation was recognized, providing a rationale for combining heat and radiation. In addition, the thermosensitivity of tumour blood vessels which collapse in transplanted tumours after ~30 min at 41.5–42.5°C was recognized. A variety of mechanisms were proposed to explain this collapse. More recently vascular collapse after photodynamic therapy, chemotherapy (*e.g.* melphalan and misonidazole, flavone acetic acid), radiotherapy and biological response modifiers (*e.g.* interferon, interleukins and TNF) has been quantified. The possibility of temporarily increasing hypoxia to enhance the effect of bioreductive drugs has also been investigated. It is now clear that indirect ischaemic cell death as a result of cessation of blood flow may be a feature of many cancer therapies. The mode of action may be common for all agents or may involve different aspects of the poor tumour vasculature. These include the rapid proliferation of the endothelial cells, their immaturity and consequent lack of differentiation, the poorly formed vessel wall, their lack of innervation or lack of organized architecture. The chaotic structure leads to unpredictable and reversible flow patterns, with areas of stasis and with arterio-venous shunts. The nutritional quality of the blood is poor at a lower pH, being depleted of essential metabolites, especially oxygen, and loaded with catabolic products of cell breakdown. The tumour cells themselves may produce procoagulant factors, and may also stimulate the endothelium to a greater procoagulant potential. It is now essential to consider these various aspects of tumour neovasculature, and use them to design therapies targeted at tumour vessels. The avalanche of tumour death (many thousands of tumour cells die from occlusion of one capillary) is not matched by cell death in normal tissues where the excess collateral circulation can render single vessel occlusion harmless. Scheduling of existing therapies to maximize the vascular effect may be quite different from the schedules that maximize individual direct cell killing, and at present this aspect is universally ignored.

1990, *The British Journal of Radiology*, *63*, 324

Book reviews

Craniospinal Magnetic Resonance Imaging. By S. J. Pomeranz, pp. xx + 677, 1989 (W. B. Saunders, Philadelphia), £78.00.
ISBN 0-7216-2428-6

Craniospinal Magnetic Resonance Imaging is a multiauthor book under the general editorship of Stephen Pomeranz. It is aimed at a wide readership of both trainees and practising radiologists and consists of 22 chapters including those on the orbit, nasopharynx and temporomandibular joint. Rather surprisingly for such a comprehensive text book there is no chapter on the paranasal air sinuses.

The first four chapters are concerned with the principles of MRI including a very complete overview of the fast scanning techniques currently used.

The clinical section on the brain and spine consisting of 15 chapters is set out in the classical disease pattern manner with two chapters devoted to paediatrics. A very large number of pathologies are covered and although primarily a text book of MRI, comparison is made in the text with computed tomography (CT). There is a little repetition of the principles of MRI in some of the earlier chapters and since these are more than adequately covered in the first four chapters, this does seem superfluous. There are, however, a large number of very useful tables.

Considering that it is a multiauthor work it reads surprisingly consistently. There is a huge bibliography which is up to date and consists of over 2000 references. The illustrations are of good quality and since the patients have been scanned on both high and low field systems, the authors have been able to compare appearances at both field strengths where appropriate.

I enjoyed reading the books and as a reference it will be invaluable. Considering what it achieves it is not particularly expensive. I feel that of all the books on MRI I have read recently this is perhaps the most useful and I can recommend it unreservedly. Although there will undoubtedly be changes in MRI practice over the next few years, this book will continue to provide the basic information necessary to build on.

D. KINGSLEY

Bone Mineral Measurements by Photon Absorptiometry: Methodological Problems. Ed. by J. Dequeker, P. Geusens and H. W. Wahner, pp. xii + 479, 1988 (Leuven University Press, Belgium), 1700 Belgian Francs.
ISBN 90-6186-275-2

This densely packed volume is based on the Second International Workshop on Methodological Problems of Photon Absorptiometry held in Belgium in 1987. It is a valuable collection of comparative and investigative studies on bone mineral measurement over the most active growth phase of its development.

The subject matter therefore ranges from radiogrammetry and single photon absorptiometry through dual photon techniques to dual X-ray absorptiometry. The latter subject was, however, only available for introductory papers at the time of workshop. Nevertheless, there is a wealth of experience contained within this book, a great deal of which will be valuable reading, even if some of the techniques do become obsolete in the next few years.

Following the theme of the workshop, the volume is divided into four parts. The first is a collection of 26 short papers on clinical application of bone mineral measurements by photon absorptiometry. The second part deals with quality control of procedures, which also includes papers on the effects of source decay and the possible effects of seasonal variation in BMC values *in vivo*. Some data on reproducibility of BMC data between laboratories and populations are particularly useful.

In part three, longitudinal measurements of bone mass and their use in monitoring treatment of osteoporosis highlight the key problem. In this technology, clinical change is often very close to the borders of reproducibility of the measurement systems: a subject which is honestly and critically reviewed.

The last part, headed "Where do we go from here?" is an assortment of short papers, and contains the three papers on dual X-ray absorptiometry. Introductory papers by Stein (of Hologic) and Mazess (Lunar Corporation) outline the performance of this improved technique. Another paper by Wahner et al compares quantitative digital radiography (QDR) with dual photon absorptiometry (DPA) for measurements of the lumbar spine, claiming a high correlation between a Lunar and a Hologic system used at the Mayo Clinic.

Also of interest in this final section was a paper from Sienna, Italy, on the place of total body dual photon absorptiometry versus separate regional measurements. This is a technique which is becoming more practical with faster X-ray systems for whole skeletal measurement.

The special interests of both the Danish and Belgian groups are well represented. Patterns of normal and abnormal bone loss by Schaadt of Copenhagen, and longitudinal changes in BMC by Dequeker's group at Leuven are well described. Some repetition occurs in this large collection of short papers, for instance one paper questions "should BMC measurements be corrected for skeletal size?" while a later paper including the same authors, presents data on the effect of normalization for skeletal size. (There is one particular difficulty for the reader, who may use this book for quick reference. The table of contents lists the papers but does not give the page numbers.) An excellent introductory section is provided by Wahner and Dequeker in which instrument characteristics are tabulated, together with diagnostic tests and phantoms.

Many of the studies reported are concerned with trends in clinical data. They also stress that "problems in comparable results from different centres, disagreement on the best measurement site, and lack of effective treatment regimen are in part responsible for the continuing controversy around these techniques".

Contributions from American and Australian workers give this volume a good international flavour. They draw attention to the specific problems facing the US investigators of bone mineral measurement. The need to prove reliability and significance of fracture risk assessment in an insurance-weighted service leads to much debate on cost-benefit of simple versus more expensive technology.

The book is good value for those who use photon absorptiometry, and it provides a wide spectrum of practical experience often lacking in a more easily read monograph. Well presented discussion sessions give the reader an excellent glimpse into the workshop itself, which has put many issues on record often missing from the manufacturer's literature.

E. F. J. RING

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Thyroid imaging using positron emission tomography—a comparison with ultrasound imaging and conventional scintigraphy in thyrotoxicosis

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Abstract. Forty-six comparative studies were performed on 41 patients with hyperthyroidism. Clinically these comprised two groups: those with Graves' disease, and those with multinodular goitre. All patients underwent an ultrasound examination and positron emission tomography (PET) using ^{124}I, then gamma camera pinhole imaging following their ^{131}I therapy administration. Although the ^{131}I pinhole imaging was not performed for diagnostic purposes, there was good correlation (78% agreement) between it and ^{124}I PET in determining relative lobe size. Hence either imaging modality could be used as an indicator of the relative radiation dose delivered to each thyroid lobe at a macroscopic level. In terms of gland morphology the PET images corresponded well to the high resolution ultrasound images (78% agreement), unlike the pinhole images which correlated poorly (only 28% agreement). The results showed that PET imaging gives better anatomical and physiological detail than ^{131}I pinhole imaging. In 77% of cases where the pinhole image showed a uniform distribution of radioisotope, the improved spatial resolution of the PET images revealed non-homogeneous distribution indicating a non-uniform distribution of radiation dose. Since all dosimetry calculations are based on the assumption of uniform distribution of radioiodine, this non-uniformity could possibly have important consequences in the outcome of radioiodine therapy in thyrotoxicosis.

At the present time the current methods of imaging the thyroid gland are ultrasound and conventional scintigraphy (using a gamma camera with a pinhole collimator). While the latter offers physiological information about the gland, it lacks the high spatial resolution obtained with ultrasound which provides detailed anatomical information. Positron emission tomography (PET) is a new and rapidly evolving technique offering improved lesion to normal tissue contrast over conventional scintigraphy. Hence the main purpose of this study was to evaluate the relative clinical value of the three imaging modalities: PET, ultrasound and conventional scintigraphy.

The use of high resolution ultrasound in the investigation of thyroid disease is well established. Using a 10 MHz probe, the resolution is excellent with lesions of 2 mm being identified (Simeone et al, 1982). The features of solitary nodules, multinodular goitres and texture change in general thyroid disturbances such as Graves' disease have been extensively studied (Simeone et al, 1982; Katz et al, 1984; Dumitriu & Gudovan-Călin, 1985; James & Charboneau, 1985; Woestyn et al, 1985). These studies attempted to relate the ultrasonic findings to the pathological findings. It was noted (Simeone et al, 1982) that in dealing with six small lesions of between 2–6 mm which were detected by ultrasound and removed, only half were detected by radioisotope scintigraphy: these lesions were papillary carcinomas on histology. Other authors (Katz et al, 1984) have commented on the failure of scintigraphic images to detect lesions identified by ultrasound. With a resolution of 2 mm, ultrasound has led to the discovery of nodules in otherwise "normal" thyroid glands, occurring in 19% in a series of 300 patients (Woestyn et al, 1985). Other authors have noted similar findings and documented the failure of scintigraphy to detect lesions of less than 1.5 cm (Pinedo et al, 1984). Indeed the high resolution of ultrasound now rivals the macroscopic inspection by an experienced pathologist of a thyroid gland sectioned serially (Caselli & Feggi, 1984; Hay et al, 1984).

With the improvement in ultrasonic resolution and the advent of fine needle aspiration cytology, the clinical value of scintigraphic imaging of the thyroid gland has

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been called into question. However, since ultrasound cannot indicate the functional status of thyroid nodules and since hyperfunction makes cancer unlikely, it is worth comparing PET (with its higher spatial resolution and higher contrast than conventional scintigraphy) with ultrasound to re-evaluate the relative merits of ultrasound and scintigraphy.

The original equipment used for radioisotope imaging of the thyroid was the rectilinear scanner. The spatial resolution of this device was dependent on the collimator design: typical values of 8 mm and 12 mm for the spatial resolution (full width at half-maximum of the line spread function in the focal plane) were achievable with $^{99}Tc^{m}$ and ^{131}I respectively. When gamma cameras became the instruments of choice, optimized for $^{99}Tc^{m}$ imaging, rectilinear scanning of the thyroid gland was replaced by pinhole collimator scintigraphy. The spatial resolution achieved with pinhole scintigraphy is again dependent on collimator design (in this case the diameter of the pinhole), on the radioisotope and the source-to-collimator distance. Typical values for the geometric collimator resolution are 3.5–7.5 mm for hole diameters of 3–6 mm at distances of 5–10 cm.

Various techniques have been employed to improve radioisotope imaging of the thyroid. These have included computer-assisted enhancement (Armstrong et al, 1975), the use of a seven-pinhole collimator (Telepak et al, 1983) and single-photon emission tomography (SPECT) (Webb et al, 1986; Chen et al, 1988). Although SPECT, like PET, offers improved contrast over planar imaging, the spatial resolution achieved by SPECT is of the order of 10 mm at best, being limited by collimator design and system sensitivity. In contrast, the intrinsic special resolution of PET systems is of the order of 2–3 mm while in practice a spatial resolution of 5–7 mm can be achieved with a high sensitivity system.

PET imaging of the thyroid has already been compared with conventional pinhole scintigraphy by two groups. Frey et al (1985a) found that 15 out of 16 patients with Graves' disease had homogeneous uptake by ^{123}I pinhole imaging while 12 of these were non-homogeneous by ^{124}I PET imaging. In 25 patients with multinodular goitre the conventional scintigram was abnormal in 18 while the PET was abnormal in all cases. A further study by Frey et al (1985b) of 38 patients with either Graves' disease or multinodular goitre also showed non-homogeneous uptake in PET thyroid images while ^{131}I pinhole images showed uniform distribution. Occasionally, because of the improved image contrast provided by PET over pinhole imaging, the clinical diagnosis was changed: while the ^{124}I pinhole image suggested a solitary cold nodule, PET showed multiple areas of abnormal uptake indicative of a multinodular goitre (Frey et al, 1986).

Similar results were reported in a previous study carried out by our group (Ott et al, 1987). In 22 patients there were no cases where non-homogeneous uptake was detected by ^{131}I pinhole imaging and not by ^{124}I PET. However, in five out of 18 patients with apparently uniform uptake on the ^{131}I pinhole image, non-uniformity was demonstrated by PET.

In the previous PET *versus* pinhole studies summarized above, ultrasound imaging was not performed for comparison. It is the main purpose of this study to correlate the findings on ^{124}I PET imaging with those on ultrasound. The group of patients selected for this study were those undergoing ^{131}I therapy for hyperthyroidism and who were already taking part in a dose/response study. As the ^{131}I pinhole image was automatically available this was included for comparison with the ^{124}I PET and ultrasound findings. However, it was felt unfair to include additional ^{123}I or $^{99}Tc^{m}$ pinhole imaging which ideally would be included for completeness as the patients already had to attend hospital for two extra days for the dosimetry study.

Materials and methods

Forty-one patients routinely referred to the Thyroid Unit for treatment of hyperthyroidism were evaluated. Five patients received a second treatment with radioiodine, so 46 comparative studies were performed in all. The patients were divided into two groups on the basis of clinical examination and antibody status, using the thyrotrophin receptor antibody (TRAB). From these results, patients were divided into those with Graves' disease (30 patients, 34 studies) and those with multinodular goitre (11 patients, 12 studies). The age and sex distributions of the patients in each group are presented in Table I.

All patients underwent ultrasound examination using an Acuson real time scanner with a 5 MHz linear array probe. Selected images were taken in axial and longitudinal planes. Echotexture was assessed as normal, abnormal (*i.e.* coarse) or nodular. Because of the difficulty in accurately measuring thyroid volume using ultrasound, no attempt was made to assess lobe size.

The PET images were acquired using a multiwire proportional chamber positron camera (Ott et al, 1988) 24 h after oral administration of 15 MBq $Na^{124}I$. The sensitivity of this system is such that 500 000 coincidence events were acquired in about 20 min. The amount of smoothing incorporated into the reconstruction of the PET data was determined from experiments using thyroid-shaped phantoms, uniformly filled with ^{124}I. The value of the smooth parameter was chosen to be neither too high so that noise dominated the images nor too low so that the images were over smooth with a subsequent loss of spatial resolution. Figure 1 shows examples of the effect of different values of the smoothing parameter on the images of a thyroid-shaped phantom.

Conventional scintigraphy was performed using either a Searle HP37 gamma camera with a high-energy

Table I. Diagnosis, sex and age distribution of the 41 patients studied

Diagnosis	Number	Sex	Age range (years)	Median age (years)
Graves'	30	22F, 8M	32–79	55
Multinodular	11	9F, 2M	36–87	63

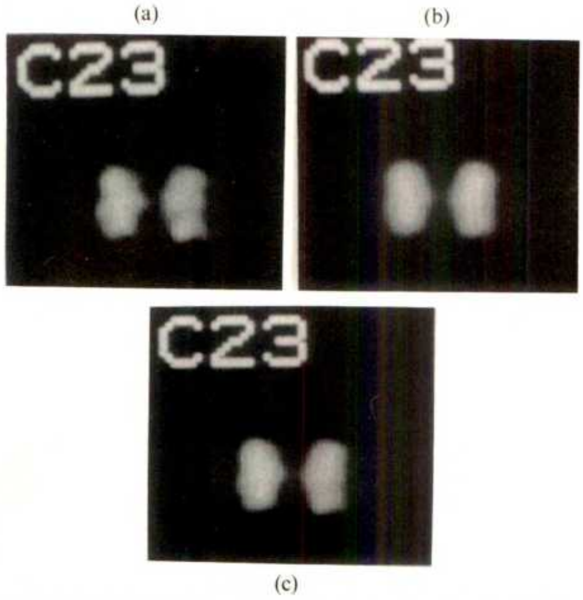

Figure 1. Effects of different values of the smoothing parameter on the images of a thyroid-shaped phantom: (a) too high; (b) too low; (c) optimum.

pinhole collimator (4 mm diameter) or a GE 400A camera with a medium-energy pinhole collimator (3 mm diameter). The pinhole image was acquired 24 h after oral administration of (typically) 75 or 400 MBq Na^{131}I for the treatment of Graves' disease or multinodular thyrotoxicosis respectively. Acquisition times were typically less than 5 min for 150 000 detected events.

The isotope images (both pinhole and PET) were assessed in terms of relative lobe size. In addition, the isotope distribution was classified as being either homogeneous or non-homogeneous.

Results

Figures 2–6 show comparative images for five patients included in this study. The results of all the intercomparisons are summarized in Tables II and III.

Both groups show good correlation between pinhole and PET imaging in assessing relative lobe size with agreement in 27 out of 34 studies with Graves' disease, and 9 out of 12 with multinodular goitre, the overall agreement being 36 out of 46 (78%).

In terms of the distribution of isotope with pinhole and PET imaging compared with ultrasound echotexture, there was a striking lack of correlation between the pinhole images compared with either the ultrasound or PET images. However, there was good correlation between PET and ultrasound. In the Graves' group 27 out of 34 studies (79%) positively correlated between ultrasound and PET: in only seven (21%) did the ultrasound and pinhole imaging correlate and in only 12 studies out of 34 (35%) did the pinhole and PET images agree.

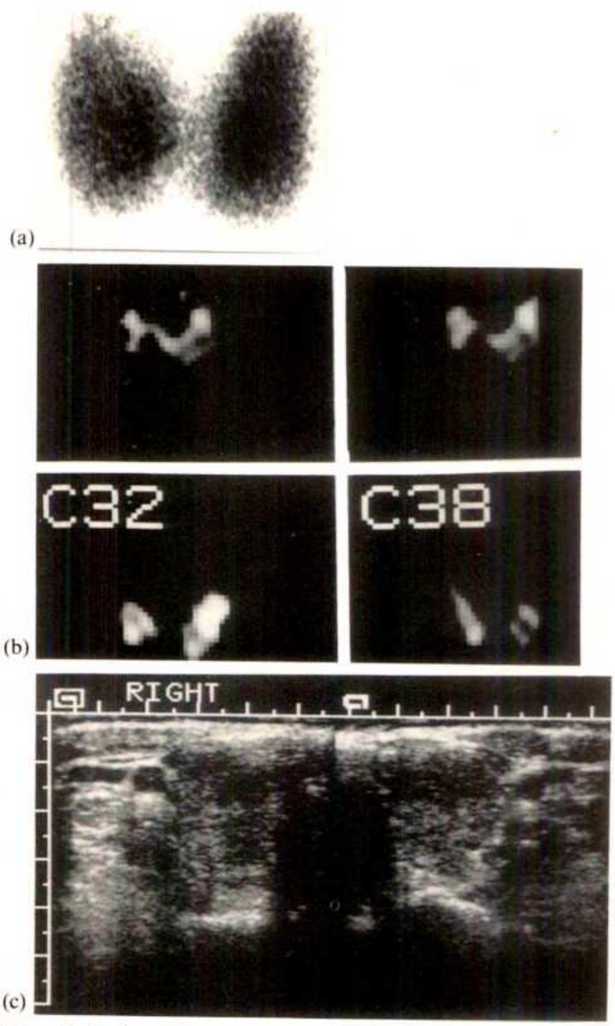

Figure 2. Patient EL with Graves' disease: pinhole image (a) shows homogeneous uptake but PET image (b) shows non-homogeneous uptake correlating with the coarse texture seen on the transverse-section ultrasound (c).

A similar pattern was observed in the multinodular group with positive correlation between ultrasound and PET in 11 out of 12 studies (92%), but only 6 out of 12 (50%) between ultrasound and pinhole imaging. In 7 out of 12 (58%) there was agreement between pinhole and PET.

Of the 30 studies which were classified as nodular on ultrasound, 28 (93%) were classified as having non-homogeneous PET images. It is interesting to note that the other two patients with a normal PET image had only small lesions of less than 5 mm on ultrasound: one case demonstrated a single small lesion in one lobe (Fig. 6) and the other showed multiple small lesions bilaterally.

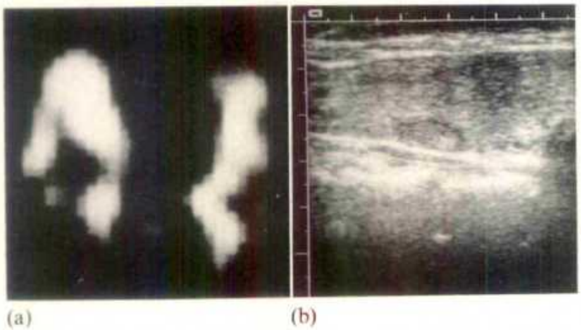

Figure 3. Patient JL with multinodular goitre: PET image (a) is grossly abnormal and multiple nodules are seen on the ultrasound (b).

Discussion

The relatively good correlation of 78% between ^{131}I pinhole and ^{124}I PET imaging in assessing relative lobe size shows that, if PET is not available, pinhole imaging is a useful indicator of the relative radiation dose delivered to each thyroid lobe at a macroscopic level. However, if PET is available, the complete set of tomographic images enables an estimate to be made of the absolute volume of each thyroid lobe and of the whole gland. The latter can be used in the determination of radiation dose delivered by radioiodine therapy (Ott et al, 1987).

The previous findings of the comparisons between PET and pinhole imaging by Frey et al (1985a,b, 1986)

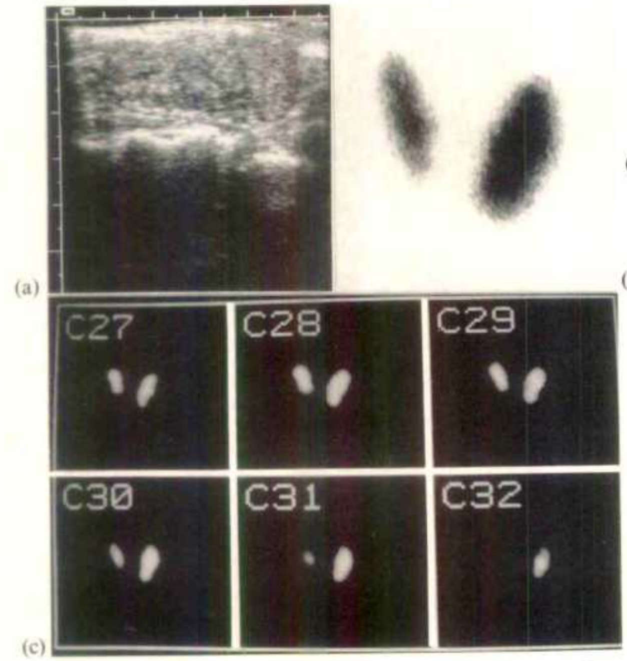

Figure 4. Patient MC with multinodular goitre: ultrasound (a) shows small nodules not identified on either the pinhole (b) or PET (c).

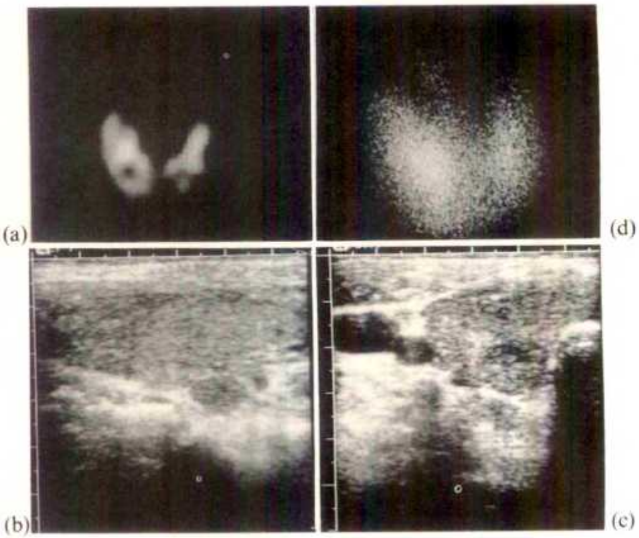

Figure 5. Patient JM with Graves' disease: PET image (a) clearly shows a focal defect in the lower pole of each lobe, agreeing with the ultrasound findings; (b) left longitudinal and (c) right transverse. In contrast, the pinhole image (d) identifies only a poorly defined count-deficient area in the left lobe.

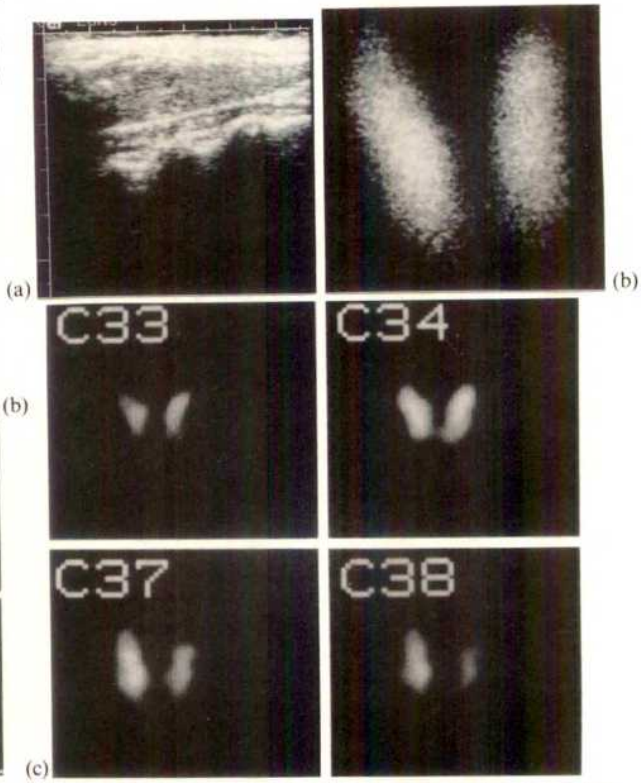

Figure 6. Patient MR with Graves' disease: a single small lesion is visualized in the right lobe on longitudinal ultrasound (a) but is not seen on pinhole (b) or PET (c).

Table II. Comparison between PET and pinhole imaging with respect to determination of relative lobe size

			PET RESULTS		
			R > L	Equal size	L > R
PINHOLE RESULTS	R > L	Graves'	20	0	0
		Multinodular	5	1	0
		Total	25	1	0
	Equal size	Graves'	4	2	1
		Multinodular	0	3	1
		Total	4	5	2
	L > R	Graves'	1	1	5
		Multinodular	1	0	1
		Total	2	1	6

Key: R > L = right lobe much larger than left lobe; L > R = left lobe much larger than right lobe.

Table III. Comparison between ultrasound, PET and pinhole imaging with respect to echo-texture and isotope distribution

(a) PET *versus* ultrasound

			PET RESULTS	
			Normal	Non-homogeneous
ULTRASOUND RESULTS	Normal	Graves'	1	1
		Multinodular	0	0
		Total	1	1
	Coarse	Graves'	5	9
		Multinodular	0	0
		Total	5	9
	Nodular	Graves'	1	17
		Multinodular	1	11
		Total	2	28

(b) PET *versus* pinhole

			PET RESULTS	
			Normal	Non-homogeneous
PINHOLE RESULTS	Normal	Graves'	7	22
		Multinodular	1	5
		Total	8	27
	Non-homogeneous	Graves'	0	5
		Multinodular	0	6
		Total	0	11

(c) Pinhole *versus* ultrasound

			PINHOLE RESULTS	
			Normal	Non-homogeneous
ULTRASOUND RESULTS	Normal	Graves'	2	0
		Multinodular	0	0
		Total	2	0
	Coarse	Graves'	12	2
		Multinodular	0	0
		Total	12	0
	Nodular	Graves'	15	3
		Multinodular	6	6
		Total	21	9

and Ott et al (1987) are borne out in the present study, although it must be appreciated that pinhole imaging was performed not for diagnostic purposes and therefore not using radionuclides such as ^{123}I or ^{99}Tc^{m} which would have provided higher quality images. However, we have also been able to correlate our results with high resolution ultrasound, which is felt to have a resolving power similar to macroscopic serial sectioning of the gland. From our results it appears that not only can nodules and multinodular change be seen but that texture changes apparent with ultrasound can be appreciated with PET imaging.

The classical appearance of Graves' disease is of an enlarged gland with diffuse and regular distribution of tracer. The fact that most of the patients in this study with Graves' disease revealed non-homogeneous tracer distribution with PET and/or abnormal (coarse or nodular) echotexture with ultrasound means that there is probably a spectrum of tracer distribution varying from non-homogeneous to uniform and that the classical description for Graves' disease based on conventional scintigraphy should be modified. It is accepted that this range of appearances is of little relevance to the clinical diagnosis of Graves' disease which is normally made from physical findings and antibody status. However, it is possibly relevant to the outcome of low dose radioiodine therapy (Hoskin et al, 1985; Lowdell et al, 1985). Dosimetry calculations (Ott et al, 1987) are based on the assumption that radioiodine is uniformly distributed throughout the thyroid: non-uniformity of uptake could help to explain why the end result of radioiodine therapy is so unpredictable.

The improved resolution of PET compared with pinhole scintigraphy could also have implications for patients with multinodular goitre or thyroid cancer. PET enables smaller lesions to be detected and therefore may enable an earlier diagnosis of multinodular goitre to be made. This disease is always benign whereas a single cold lesion carries a significant risk of carcinoma (Atkins, 1975). In addition, the amount of ^{131}I administered for therapy is determined by the presence or absence of nodules. If multiple nodules are present and if the administered activity is assessed on overall gland size rather than functioning volume, the clinical outcome of euthyroidism is less likely to be achieved. These implications for patient management will only be fully realized if PET becomes more widely available (Ott, 1989).

In the investigation of thyroid disease, pinhole gamma camera imaging can result in well-known artifacts. Although ultrasound images offer excellent anatomical detail, their interpretation can be more difficult compared with scintigrams which are often still more acceptable to the referring physician. PET can determine physiological activity with a resolution which is potentially similar to that of ultrasound imaging, although the former is currently available only in specialist centres. This study demonstrates that PET is superior to pinhole imaging of the thyroid and is a useful research tool which can aid in the understanding of disease and the rationalization of treatment.

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References

Armstrong, D. I., Rogers, T. G. H. & Brownlie, B. E. W., 1975. Computer-assisted thyroidal technetium uptake measurement using a short pinhole-to-surface distance. *American Journal of Roentgenology, 123*, 60–66.

Atkins, H. L., 1975. The thyroid. In *Clinical Scintillation Imaging*, 2nd edn., ed. by L. M. Freeman and P. M. Johnson (Grune and Stratton, New York).

Caselli, M. & Feggi, L. M., 1984. Ultrasonic demonstration of small thyroid nodules. *Lancet, 1*, 508.

Chen, J. J. S., LaFrance, N. D., Allo, M. D., Cooper, D. S. & Ladenson, P. W., 1988. Single photon emission computed tomography of the thyroid. *Journal of Clinical Endocrinology and Metabolism, 66*, 1240–1246.

Dumitriu, L. & Gudovan-Călin, E., 1985. Endocrine diagnosis by ultrasound. I. The thyroid, parathyroid and adrenal glands. *Revue Roumaine de Médecine, Série Endocrinologie, 23*, 3–12.

Frey, P., Townsend, D., Mégevand, R., Spiliopoulos, A., Huber, O., Donath, A. & Jeavons, A., 1985a. Tomographic imaging of the human thyroid with a positron camera before and after partial thyroidectomy. *European Surgical Research, 17*, 347–351.

Frey, P., Townsend, D., Jeavons, A. & Donath, A., 1985b. In vivo imaging of the human thyroid with a positron camera using ^{124}I. *European Journal of Nuclear Medicine, 10*, 472–476.

Frey, P., Townsend, D., Flattet, A., De Gantard, R., Widgren, S., Jeavons, A., Christin, A., Smith, A., Long, A. & Donath, A., 1986. Tomographic imaging of human thyroid using ^{124}I. *Journal of Clinical Endocrinology and Metabolism, 63*, 918–927.

Hay, I. D., Reading, C. C. & Charboneau, J. W., 1984. High-resolution real-time ultrasonography and unsuspected micronodular thyroid disease. *Lancet, 1*, 916.

Hoskin, P. J., Spathis, G. S., McCready, V. R., Cosgrove, D. O. & Harmer, C. L., 1985. Low-dose radioiodine given six-monthly in Graves' disease. *Journal of the Royal Society of Medicine, 78*, 893–898.

James, E. M. & Charboneau, J. W., 1985. High frequency (10 MHz) thyroid ultrasonography. *Seminars in Ultrasound, CT and MR, 6*, 294–309.

Lowdell, C. P., Dobbs, H. J., Spathis, G. S., McCready, V. R., Cosgrove, D. O. & Harmer, C. L., 1985. Low-dose ^{131}I in treatment of Graves' disease. *Journal of the Royal Society of Medicine, 78*, 197–202.

Katz, J. F., Kane, R. A., Reyes, J., Clarke, M. P. & Hill, T. C., 1984. Thyroid nodules: sonographic–pathologic correlation. *Radiology, 151*, 741–745.

Ott, R. J., Batty, V., Webb, S., Flower, M. A., Leach, M. O., Clack, R., Marsden, P. K., McCready, V. R., Bateman, J. E., Sharma, H. & Smith, A., 1987. Measurement of radiation dose to the thyroid using positron emission tomography. *British Journal of Radiology, 60*, 245–251.

Ott, R. J., Marsden, P. K., Flower, M. A., Webb, S., Cherry, S. & McCready, V. R., 1988. Clinical PET with a large area MWPC PET camera (MUP-PET). *Nuclear Instruments and Methods in Physics Research, A269*, 436–442.

Ott, R. J., 1989. Nuclear medicine in the 1990s: a quantitative physiological approach. *British Journal of Radiology, 62*, 421–432.

Pinedo, J. I., Marana, G., Alonso, M. & Berrocal, J. O., 1984. Echographic thyroid nodules not detected on radionuclide scintigraphy. *Lancet, 2*, 39–40.

Simeone, J. F., Daniels, G. H., Mueller, P. R., Maloof, F., van Sonnenberg, E., Hall, D. A., O'Connell, R. S., Ferrucci, J. T., Jr. & Wittenberg, J., 1982. High-resolution real-time sonography of the thyroid. *Radiology, 145*, 431–435.

Telepak, R. J., Bunker, S. R., Lancaster, J. L., Hartshorne, M. F. & Blumhardt, R., 1983. Another use of the seven-pinhole collimator. Routine non-tomographic imaging of the thyroid. *Clinical Nuclear Medicine, 8*, 163–164.

Webb, S., Flower, M. A., Ott, R. J., Broderick, M. D., Long, A. P., Sutton, B. & McCready, V. R., 1986. SPECT imaging and volume estimation of the thyroid using fan-beam geometry. *British Journal of Radiology, 59*, 951–955.

Woestyn, J., Afschrift, M., Schelstraete, K. & Vermeulen, A., 1985. Demonstration of nodules in the normal thyroid by echography. *British Journal of Radiology, 58*, 1179–1182.

1990, *The British Journal of Radiology*, *63*, 331–332

The ultrasound cystodynamogram—a new radiological technique

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Abstract. Voiding dysfunction may be assessed using the intravenous urodynamogram (IVUD) or combined with pressure studies in the videocystometrogram (VCMG). However, VCMG requires bladder catheterization and voiding in public which often leads to inhibition of sphincter relaxation. For this reason the urinary flow rate measurement performed in private is more representative of the true voiding pattern. The ultrasound cystodynamogram (USCD) evaluates the bladder capacity, mean and maximum flow rates, flow pattern and post-micturition residual. The diagnostic capability of USCD was studied in 116 consecutive cases 46 of whom had also had VCMG. Comparison of the data obtained using both techniques revealed no significant difference. USCD has proved to be accurate, safe and reproducible and is of particular value in patient follow-up.

Patients with voiding problems may present with a variety of non-specific clinical symptoms (Siroky et al, 1979). The videocystometrogram (VCMG) is recognized to be the "gold standard" in urodynamic assessment, but it is increasingly recognized that not all patients require such an invasive study (Barton & Sherwood, 1983). The intravenous urodynamogram (IVUD) was developed as a modification of the excretory urogram (EU) as an initial screening test for patients with urinary tract dysfunction (Turner-Warwick et al, 1979). Following the 20 min full length radiograph a diuretic (*e.g.* frusemide) is injected and when the patient feels the bladder is naturally full, a flow rate in private is obtained followed by an immediate post-micturition film.

The ultrasound cystodynamogram (USCD) is similar to the IVUD with ultrasound assessment of pre- and post-micturition bladder volumes. Its advantages are that it does not need contrast administration or ionizing radiation and that it can be repeated as often as is required.

Patients and methods

One hundred and sixteen consecutive patients (70 male, 46 female) with voiding difficulties were studied over a 9-month period. The age range was from 14 to 84 years and with a mean of 61 years.

The clinical groups comprised the follow-up of patients after prostatectomy (25), colposuspension (12), urethral dilatation (13), and the assessment of patients with detrusor failure (29), detrusor-sphincter dysynergia (16), urethral reconstruction (4) and other voiding disorders.

Patients with physiologically full bladders were assessed using a standard technique (Poston et al, 1983), *i.e.* the bladder volume in millilitres is $0.7\,HDW$ (D = depth in sagittal plane, H = maximum diameter in sagittal plane and W = maximum transverse diameter in transverse plane; all measurements in centimetres). Patients then voided into a standard flow-meter which allowed measurement of the mean and maximum flow rates and assessment of the flow pattern. The post-micturition bladder volume, if present, was then measured.

Results

The values for the average pre-voiding and post-voiding bladder volumes and maximum flow rates are shown in Table I for each of the clinical groups. These values were correlated with those obtained at VCMG in the 46 patients who had undergone both studies and were found to be highly statistically significant. The correlation coefficient (r) was 0.639, 0.847 and 0.356 for

Table I. Average bladder volumes and maximum flow rate for each clinical group

	Pre-voiding volume (ml)	Post-voiding volume (ml)	Maximum flow (ml/s)
Post-prostatectomy	341	82	17.1
Post-colposuspension	641	289	18.5
Post-urethral dilatation	439	123	19.2
Long term detrusor failure	479	179	14.1
Detrusor-sphincter dyssynergia	550	308	18.0
Urethral reconstruction	309	36	21.3
Other	594	254	26.5

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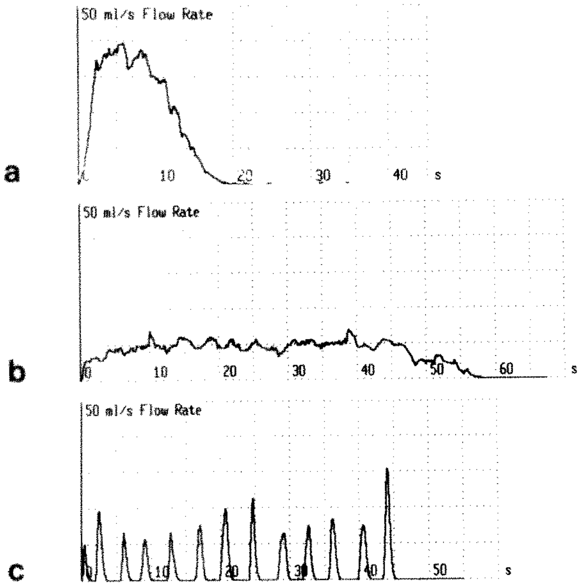

Figure 1. (a) Normal "bell-shaped" uroflow curve. (b) "Plateau" configuration of obstruction. (c) Detrusor failure: saw-tooth pattern due to abdominal straining.

the pre-voiding volume, the post-voiding volume and the maximum flow rate respectively.

Several "classical" flow patterns were identified (Fig. 1b and 1c) and the normal flow pattern (Fig. 1a) is shown for comparison.

Discussion

Uroflowmetery is widely used in clinical urological practice but not by radiologists. The USCD provides significant but limited urodynamic information sufficient to render VCMG unnecessary in some groups of patients. It is particularly helpful in the follow-up of patients with known voiding problems. Analysis of uroflow patterns, mainly in bladder outflow obstruction of differing aetiologies has been reported (Tripathi & Sridhar, 1983). The normal uroflow curve (Fig. 1a) is bell shaped and approximately symmetrical. The average maximum flow rate is 32 ml/s and the mean flow rate is 18 ml/s. Females have slightly higher maximum and mean flow rates than males, owing to the lower resistance of the female urethra (Christmas et al, 1989). The normal patient voids to completion.

The uroflow pattern in obstruction (Fig. 1b) demonstrates a plateau configuration with a prolonged voiding time and reduced maximum flow rate. In our group of obstructed patients (following prostatectomy, colposuspension and urethral dilatation) the average post-voiding residue was 142 ml.

In the group with detrusor failure (secondary to chronic outflow obstruction) there was an increase in the pre-voiding volume and a large residual averaging 179 ml. The uroflow pattern was "sawtooth" owing to abdominal straining in an attempt to empty the bladder (Fig. 1c).

The patients with detrusor/sphincter dyssynergia, all with multiple sclerosis, had large pre- and post-voiding bladder volumes (550 ml and 308 ml respectively). Their uroflow chart revealed a low-flow pattern with some superimposed straining.

In the small group with urethral reconstruction there was a normal, bell-shaped curve which had a lowered peak (maximum flow 19 ml/s) and there was a small residual volume of urine.

The urinary flow rate is influenced by the initial bladder volume, voiding detrusor pressure and outflow resistance. However, consistent values can be obtained in the same individual unless the bladder volume is less than 150 ml (Smith, 1966). Some doubt has been expressed about the accuracy of ultrasound bladder volume measurements (Keily et al, 1987) but in our group we found the measurements to be accurate and reproducible. In addition, ultrasound allows assessment of the soft tissues of the pelvis rather than just the contrast-filled cavities (Porena et al, 1987).

The USCD has been most helpful in the follow-up of post-operative patients and is a simple method of assessing changes in voiding efficiency. It is a useful adjunct to VCMG since it is non-invasive, cheap, requires only basic ultrasound equipment and is well tolerated by patients. However, VCMG remains the "gold standard" for more complex cases requiring simultaneous pressure studies.

References

Barton, E. J. & Sherwood, T., 1983. Video urodynamic studies and clinical outcome. *British Journal of Radiology, 56*, 805–807.

Christmas, T. J., Chapple, C. R., Dixon, P. J., Buckley, J. F., Milroy, E. J. G. & Turner-Warwick, R. T., 1989. The effect of abdominal straining on the urinary flow rate in normal subjects. (Personal communication.)

Keily, E. A., Hartnell, G. G., Gibson, R. N. & Williams, G., 1987. Measurement of bladder volume by real-time ultrasound. *British Journal of Urology, 60*, 33–35.

Porena, M., Vespasiani, G., Virgili, G., Lombi, R., Mearini, E., Rosi, P. & Micali, F., 1987. Real-time transrectal sonographic voiding cystourethrography. *Urology, 30(2)*, 171–175.

Poston, G. J., Joseph, A. E. A. & Riddle, P. R., 1983. The accuracy of ultrasound in the measurement of changes in bladder volume. *British Journal of Urology, 55*, 361–363.

Siroky, M. B., Olson, C. A. & Krane, R. J., 1979. The flow rate nomogram: I Development. *British Journal of Urology, 122*, 665–668.

Smith, J. C., 1966. The measurement and significance of the urinary flow rate. *British Journal of Urology, 30*, 701–705.

Tripathi, V. N. P. & Sridhar, M., 1983. Urodiagrams: a new method of uroflow pattern analysis. *Journal of Urology, 130*, 309–311.

Turner-Warwick, R., Whiteside, C. G., Milroy, E. J., Pengelly A. W. & Thompson, D. T., 1979. The intravenous urodynamogram. *British Journal of Urology, 51*, 15–18.

1990, *The British Journal of Radiology*, *63*, 333–336

Congenital biliary dilatation: a spectrum of disease detailed by ultrasound

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Abstract. Recently we have examined six children with the diagnosis of choledochal cyst who demonstrate a greater spectrum of biliary involvement than expected. Classically choledochal cysts have been divided into types and subtypes based on the configuration of common bile duct dilatation; however, this simplified information is misleading since surgical management is dependent on the exact extent of intrahepatic and extrahepatic biliary abnormalities. The pre-operative ultrasound examination must be meticulous to provide enough pertinent anatomic details. Much of the intrahepatic anatomy is not visualized at surgery nor on the operative cholangiograms where reflux of contrast into the intrahepatic ducts may not be consistently achieved.

Our recent patients with choledochal cyst emphasize the spectrum of biliary abnormality and the inadequacy of the type and subtype categorizations recommended in the ultrasound literature.

Choledochal cysts were initially categorized into three types dependent on the anatomical location of the cyst-like dilatation of the common bile duct: concentric dilatation, eccentric dilatation and choledochocoele (Alonso-Lej et al, 1959). Multiple cystic dilatations of the intrahepatic biliary radicles, Caroli's disease, were then added as a separate category to the classification (Bass & Cremin, 1976). The association of cystic dilatation of the common bile duct and intrahepatic dilatation has been described but the reports in the literature suggest this to be rare and in older children (Valayer & Alagille, 1975; Todani et al, 1978). Various subtypes have been described (Todani et al, 1978; Kangarloo et al, 1980). With the increasing use of ultrasound in patients presenting with cholestasis there has been an increased frequency of cases of choledochal cyst noted with intrahepatic disease (DiPietro & Taylor, 1980; Kangarloo et al, 1980; Han et al, 1981; Mettler et al, 1981).

Several hypotheses concerning the etiology of choledochal cyst have been published. More recent ones support the suggestion of a spectrum of disease. Most authors agree that it is a congenital condition. An anomalous union between the common bile duct and the pancreatic duct has been documented in patients with choledochal cyst. In this anomaly, the pancreatic duct inserts into the distal common bile duct quite proximally, and at a more acute angle than is seen in normal individuals. This anomalous union of the main pancreatic duct with the common bile duct promotes reflux of pancreatic enzymes into the biliary tree (Kimura et al, 1978; Jona et al, 1979; Todani et al, 1985). The degree and extent of dilatation of the biliary tree is believed to be secondary to inflammation with reactive fibrosis and subsequent dilatation and can be extremely variable.

Patients and methods

Six patients with choledochal cyst have been diagnosed at our institution between 1985 and 1987. The age of the patients ranged from 3 weeks to 17 years; five of them were 3 years of age or less. Four of the patients presented with jaundice and two had abdominal pain. One patient also had increased serum levels of hepatocellular enzymes and was shown to have cirrhosis on two separate liver biopsies elsewhere. Another patient had recurrent sepsis prior to being seen at our hospital. There were three boys and three girls; there were no Asian children in this series. Operative findings, operative cholangiography and pre-operative ultrasound studies have been reviewed.

Results

High resolution pre-operative real-time ultrasound was performed on all six patients with congenital cystic dilatation of portions of the biliary tree. Three of the six children had marked cyst-like dilatation of the common bile duct: one a concentric dilatation, one an eccentric dilatation and one a choledochocoele (Fig. 1a). The child with concentric dilatation had additional irregular beaded dilatation of the cystic duct, common hepatic duct and right and left hepatic ducts (Fig. 1b).

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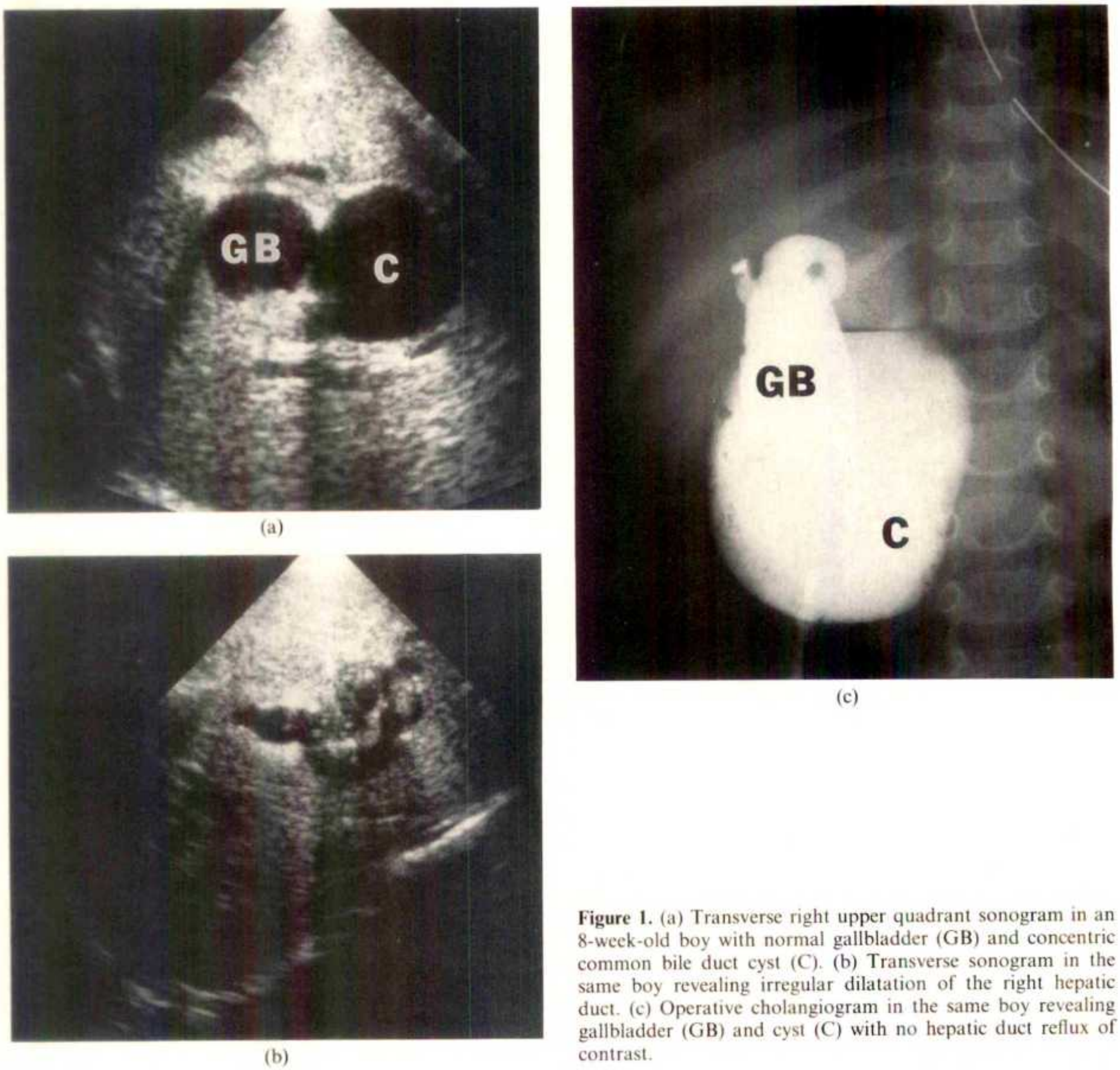

(a)

(b)

(c)

Figure 1. (a) Transverse right upper quadrant sonogram in an 8-week-old boy with normal gallbladder (GB) and concentric common bile duct cyst (C). (b) Transverse sonogram in the same boy revealing irregular dilatation of the right hepatic duct. (c) Operative cholangiogram in the same boy revealing gallbladder (GB) and cyst (C) with no hepatic duct reflux of contrast.

The other three (3–10 weeks of age) had irregular fusiform dilatation of the common bile duct which did not resemble a cyst and irregular dilatation of the common hepatic duct (Figs 2a,b). One patient had additional right hepatic duct disease and in the other two children both intrahepatic ducts were involved (Fig. 2c). Two of the patients were noted to have an annular pancreas on sonography and one was shown to have a solitary kidney.

All patients had operative cholangiograms and surgical resection of the extrahepatic abnormality with a choledochojejunostomy Roux-en-Y procedure. In the two patients with focal cyst-like lesions, cholangiography and surgery corroborated the ultrasound findings. In only one other patient was the intrahepatic anatomy demonstrated on operative cholangiography to the same extent as on ultrasound (Fig. 2d). Reflux into the intrahepatic ducts in the other patients was not consistently achieved (Fig. 1c). At surgery only the extrahepatic biliary anatomy was shown. Those portions of the biliary tree which were demonstrated confirmed the ultrasound and cholangiographic findings.

Discussion

Our group of patients reflecting current imaging procedures with choledochal cyst is very different from the large series assembled by Alonso-Lej et al (1959). All patients had a pre-operative diagnosis of choledochal cyst disease. Interestingly, half of the children were

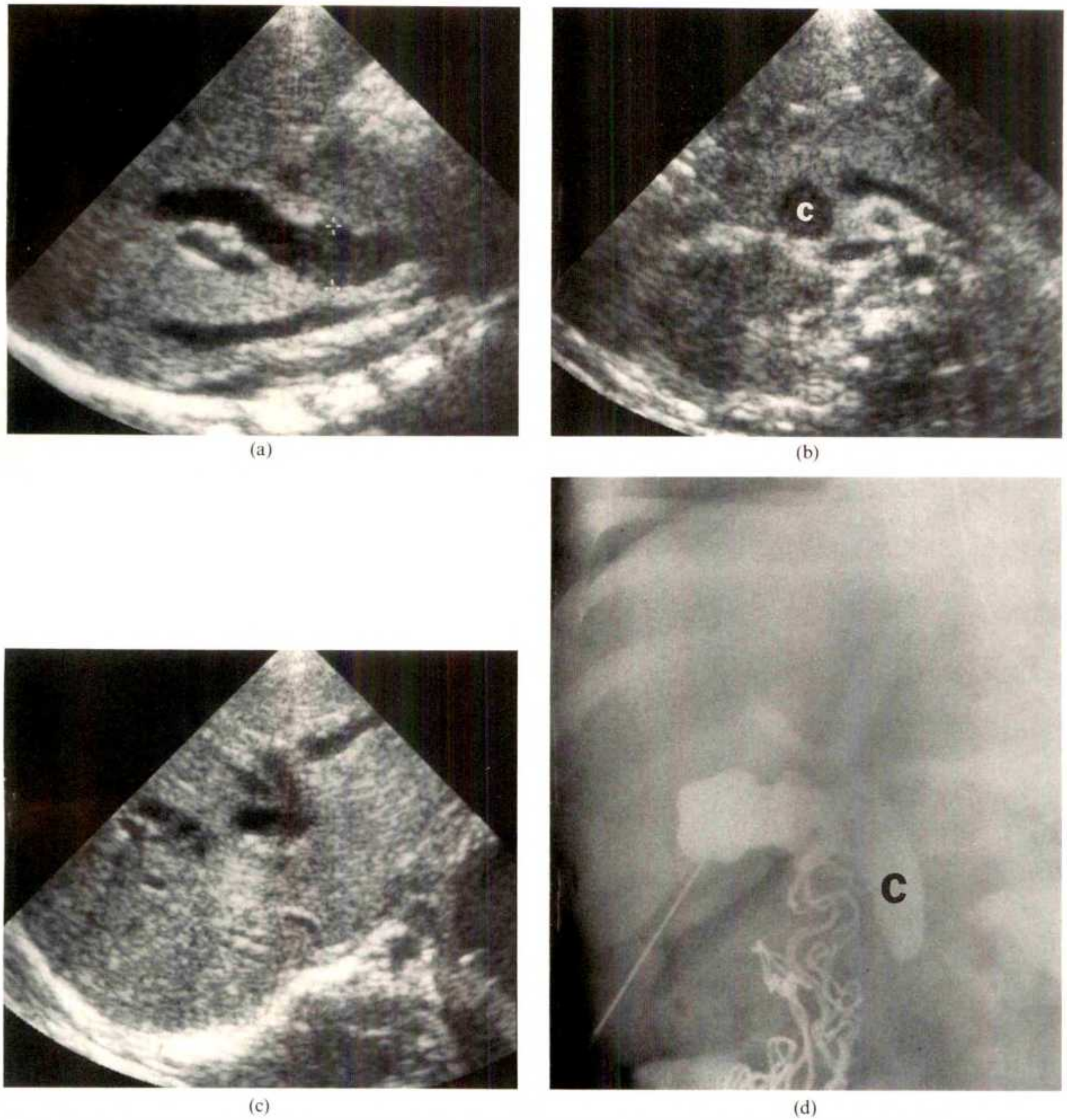
(a) (b) (c) (d)

Figure 2. (a) Oblique sonogram in a 3-week-old girl demonstrating fusiform dilatation of the common bile duct measuring 7.8 mm (between stars). (b) Transverse sonogram in the same girl reveals the dilated common bile duct in cross-section (C). (c) Transverse sonogram in the same girl reveals right and left hepatic duct dilatation. (d) Operative cholangiogram in the same patient corroborates all of the ultrasound findings of dilated common bile duct (C) and intrahepatic ducts.

boys, although a female predominance has been reported (Alonso-Lej et al, 1959; Bass & Cremin, 1976; Kangarloo et al, 1980). Only two of the six children had localized involvement of the common bile duct. Four of the children had intrahepatic disease. The children with the intrahepatic disease in our series were young (3 weeks–15 months), and not the older population previously described (Kangarloo et al, 1980).

Our results indicate that previous classifications of the type of common bile duct dilatation are often simplifications, and may be misleading for surgical planning. Surgical approach and management is currently dictated by the findings at surgery. Careful pre-operative ultrasound with detailed analysis of the dilatation to provide accurate anatomical descriptions of the extent of the disease can provide the surgeon with important information. Both the surgical approach and prognosis are directly related to the extent of involvement of the intrahepatic and extrahepatic biliary systems (Todani et al, 1978). Surgical therapy remains controversial. In view of the increasing reports of the pre-malignant potential of these cysts, excision of as much of the abnormality is advocated by some (Jona et al, 1979). Certainly, in these cases where ultrasound has demonstrated intrahepatic involvement, separation of the proximal biliary system from the pancreatic enzymes should be attempted. Ultrasound can identify pre-operatively those cases with intrahepatic disease that require careful follow-up.

Because ultrasound is recognized as the most useful imaging technique for detailed structural evaluation of the biliary system, and in particular choledochal cyst (DiPietro & Taylor, 1980; Han et al, 1981; Mettler et al, 1981), pre-operative high-resolution sonography is a necessity. The objective of ultrasonographic examination should not be simply to classify the abnormalities in an artificial and even misleading fashion, but to depict clearly the full extent of intra- and extrahepatic abnormality. Although the sonographic patterns of choledochal cyst have been categorized using modified classifications (Bass & Cremin, 1976; Todani et al, 1978), we believe these are simplifications of a complex disorder and wish to emphasize the value of accurate and complete detail in order to facilitate surgical planning in these patients.

References

Alonso-Lej, F., Rever, W. B. & Pessagno, D. J., 1959. Congenital choledochal cyst, with a report of 2, and an analysis of 94, cases. *International Abstracts of Surgery, 108*, 1–30.

Bass, E. M. & Cremin, B. J., 1976. Choledochal cysts: a clinical and radiological evaluation of 21 cases. *Pediatric Radiology, 5*, 81–85.

DiPietro, M. A. & Taylor, K. J. W., 1980. Imaging of idiopathic biliary duct dilatation. *Journal of Clinical Gastroenterology, 2*, 299–304.

Han, B. K., Babcock, D. S. & Gelfand, M. H., 1981. Choledochal cyst with bile duct dilatation: sonography and 99mTc IDA cholescintigraphy. *American Journal of Roentgenology, 136*, 1075–1079.

Jona, J. Z., Babbitt, D. P., Starshak, R. J., LaPorta, A. J., Glicklich, M. & Cohen, R. D., 1979. Anatomic observations and etiologic and surgical considerations in choledochal cyst. *Journal of Pediatric Surgery, 14*, 315–320.

Kangarloo, H., Sarti, D. A., Sample, W. F. & Amundson, G., 1980. Ultrasonographic spectrum of choledochal cysts in children. *Pediatric Radiology, 9*, 15–18.

Kimura, K., Tsugawa, C., Ogawa, K., Matsumoto, Y., Yamamoto, T., Kubo, M., Asada, S., Nishiyama, S. & Ito, H., 1978. Choledochal cyst: etiological considerations and surgical management in 22 cases. *Archives of Surgery, 113*, 159–163.

Mettler, F. A., Wicks, J. D., Requard, C. K. & Christie, J. H., 1981. Diagnostic imaging of choledochal cysts. *Clinical Nuclear Medicine, 6*, 513–518.

Todani, T., Narusue, M., Watanabe, Y., Tabuchi, K. & Okajima, K., 1978. Management of congenital choledochal cyst with intrahepatic involvement. *Annals of Surgery, 187*, 272–280.

Todani, T., Watanabe, Y., Fujii, T., Toki, A., Uemura, S. & Koike, Y., 1985. Cylindrical dilatation of the choledochus: a special type of congenital bile duct dilatation. *Surgery, 98*, 964–969.

Valayer, J. & Alagille, D., 1975. Experience with choledochal cyst. *Journal of Pediatric Surgery, 10*, 65–68.

1990, *The British Journal of Radiology*, *63*, 337–339

The role of dacryocystography in the management of patients with epiphora

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Abstract. A retrospective study has been carried out on 114 patients who have undergone dacryocystography (DCG) for epiphora, to assess the role of DCG in their management. It was found that 16/66 (24%) patients who were offered surgery after DCG refused it or were assessed as unfit for surgery, demonstrating the need for careful counselling and assessment of patients prior to investigation. The presence of lacrimal system obstruction on DCG was an important factor in determining whether a patient underwent lacrimal surgery. However, the actual level of the obstruction influenced neither the likelihood of a patient undergoing lacrimal surgery nor the form of lacrimal surgery undertaken. This suggests that, unless the surgical approach will be modified in the light of the anatomical information furnished by DCG, DCG is not necessary. Lacrimal scintigraphy would provide sufficient information for the practical management of epiphora. Syringing of the lacrimal system correlates poorly with DCG in detecting obstruction.

Epiphora is a common but rarely serious condition in ophthalmological practice. Abnormalities of the lacrimal drainage system (Fig. 1) are a common cause of epiphora. Before any radiological investigation is undertaken, the system can be syringed with saline (normally by cannulating the lower punctum). Free flow is taken to show that the system is not obstructed. It may not be possible to determine the level of obstruction by syringing; in this case an imaging technique is required: dacryocystography (DCG) or lacrimal scintigraphy. DCG is carried out by cannulating the lower punctum and injecting contrast medium into the lacrimal drainage system (Chapman & Nakielny, 1986), a technique first described by Ewing (1909). Campbell (1964) improved the technique of macrodacryocystography by geometric magnification of the image. Bone free images can be obtained by photographic or digital subtraction techniques. DCG gives precise anatomical definition of any blockage or stenosis of the system (Lloyd & Welham, 1974). It is possible to distinguish medial from lateral common canalicular obstruction.

Methods

Records of DCGs performed on patients referred for epiphora to the Diagnostic Radiology Department of the Bristol Royal Infirmary between February 1984 and January 1987 were reviewed and correlated with the medical records to ascertain both the result of syringing the lacrimal system prior to any DCG and the treatment subsequently given. The patients were grouped according to the result of their DCG:

1 Normal
2a Blockage or stenosis at the common canaliculus
2b Blockage or stenosis at the lacrimal sac
2c Blockage or stenosis at the nasolacrimal duct.

The treatment given to the patients can be grouped as follows:

1 Dacryocystorhinostomy (DCR)
2 Minor procedures—3 or 1 snip procedures,
    probing,
    retropunctal cautery,
    lacrimal gland electrolysis
3 Medical treatment—eyedrops
4 No treatment (includes those who refused surgery).

Results

A total of 180 DCGs were performed on 133 patients. Of these, six DCGs on six patients were technical failures and a further 16 DCGs on 13 patients were excluded since the subsequent clinical notes were unavailable.

The results of the DCGs in those patients who were followed up are shown in Tables I, II and III. Table I shows the results in patients with unilateral DCG, and Table II shows the results in patients with bilateral DCG. Figure 2 shows the overall number of DCGs and sites of obstruction. Table III shows the treatment given to each lacrimal system, broken down by result of DCG. Table IV compares the results of syringing lacrimal systems with the result obtained by DCG.

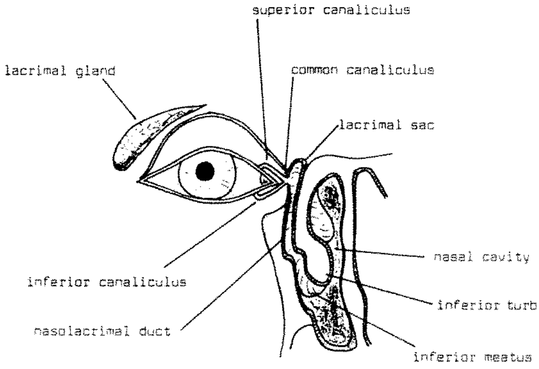

Figure 1. Anatomy of the lacrimal system.

Table I. Result of unilateral dacryocystography

1 Normal	29
2 All obstructions	41
2a blockage or stenosis at common canaliculus	15
2b at lacrimal sac	3
2c within nasolacrimal duct	23
Total:	70

Discussion

There are a number of operations which are effective in relieving epiphora caused by obstruction in the nasolacrimal system (Welham, 1987). DCR, in which an osteotomy is made in the bone separating the lacrimal sac from the nasal cavity, is used to relieve obstruction distal to the medial end of the common canaliculus so the common canaliculus drains directly into the nose. In common canalicular block it is necessary to distinguish medial from lateral blockage. Medial blockage is treated by DCR with exploration of the common canaliculus to open up mucosal adhesions. Patency is maintained by insertion of fine tubes through both the upper and lower puncta, the tubes then being passed along the lacrimal system and out through the osteotomy. They are left in position for 3–6 months and then removed through the nose. Lateral blockage is treated by a more complicated operation, canaliculodacryocystorhinostomy (CDCR), in which the common canaliculus is dissected out, the obstructed section excised, and the patent canaliculus anastomosed to the nose. Intubation is again used to maintain patency whilst the system heals and re-epithelializes.

The results of this study raise a number of points about the use of DCG in the management of patients with epiphora. On the basis of a normal DCG, lacrimal surgery in the form of DCR or CDCR would be unnecessary. Despite this, five of the 66 patients with normal DCGs underwent DCR and a further two patients were offered surgery but refused. Thus a total of seven patients (10.6% of those with normal DCGs) were offered DCR for lacrimal systems despite normal DCG. There were 18 patients with one normal and one abnormal DCG each. Ten of these 18 patients had unilateral epiphora with an abnormal DCG in the symptomatic system and a normal DCG in the asymptomatic system. While it is recognized that lacrimal pathology may be bilateral, and this may be the reason for requesting bilateral DCGs, DCG should not be requested for an asymptomatic system because no treatment would be given for it whatever the finding on DCG.

Sixty-six patients had DCGs showing obstruction amenable to lacrimal surgery. Of these, 32 underwent DCR and none underwent CDCR. Thus 34 patients did not have any form of lacrimal surgery. In 10 cases the reason for this was not clear. In eight cases, an improvement of symptoms was noted, and this may explain why they did not have surgery. Thirteen patients were offered surgery and refused it, and three patients were considered for surgery but were assessed as being unfit for an anaesthetic. These last 16 cases demonstrate the need for careful assessment and counselling of patients before submitting them to investigation. It should be noted that the proportion of patients undergoing lacrimal surgery was significantly higher ($p < 0.001$, χ^2 test) in the group of patients with abnormal DCGs

Table II. Results of bilateral dacryocystography

Side 1	Side 2	Number of patients
Normal	Normal	19
	Obstructed	
Normal	Common canaliculus	9
Normal	Nasolacrimal duct	9
Nasolacrimal duct	Nasolacrimal duct	4
Common canaliculus	Lacrimal sac	1
Common canaliculus	Common canaliculus	1
Lacrimal sac	Nasolacrimal duct	1
Total patients with bilateral DCGs		44
Total patients with one normal and one obstructed DCG		18 (41%)
Total patients with bilateral obstructed DCG		7 (16%)

Table III. Treatment given to each group

	DCR	Minor procedures	Eyedrops	Nil	Total DCGs
1. Normal	5	12	12	56	85
2a. Blockage or stenosis at common canaliculus	14	2	1	10	27
2b. Blockage or stenosis at lacrimal sac	2	0	0	3	5
2c. Blockage or stenosis at nasolacrimal duct	16	3	0	22	41

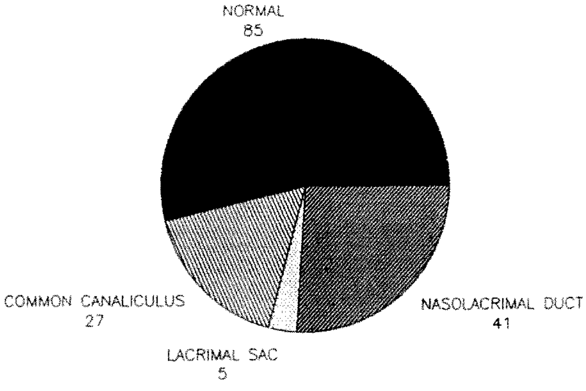

Figure 2. Site of obstruction (all DCGs).

Table IV. Comparison of the results of syringing and dacryocystography

DCG	Syringing		
	Normal	Obstructed	Not done
Normal	45	36	4
Obstructed	7	63	3

(48.5%) than in the group of patients with normal DCGs (7.6%). There was no significant difference in the proportion of patients undergoing lacrimal surgery between the groups of patients with obstruction at different sites ($p > 0.5$).

In the case of DCGs showing obstruction, it is interesting to consider the importance of the anatomical information provided. In this study, 27 cases were reported as having obstruction at the common canaliculus. They were described as medial in six cases, lateral in five, and unspecified in 16 (the number of patients who underwent DCR in these groups were three, three and eight respectively). In total, 14 DCRs were performed, all with intubation, and no CDCRs were performed. Of the five patients with lateral canalicular block, three underwent DCR with satisfactory clinical response. In the other two, no surgery was offered, and their symptoms persisted. Clearly the distinction between medial and lateral common canalicular obstruction did not in practice influence the surgical management of these patients.

Further generalizations can be made about the larger group of the 66 patients with abnormal DCGs. Thirty-two of these patients had a DCR, and all but two also had intubation. The surgical management of these patients was nearly entirely uniform, irrespective of the site of obstruction demonstrated on DCG, suggesting that the anatomical information on the level of obstruction given by DCG is not important in the management of epiphora.

The presence or absence of obstruction on DCG is important in determining whether or not a patient will have lacrimal surgery, whereas the level of obstruction is not. It is therefore arguable that a simple procedure that indicates only whether the lacrimal drainage system is patent or obstructed would provide adequate assessment of the system. Syringing of the lacrimal drainage system has already been described and it fits these criteria. However, the data in Table IV show that the results of syringing correlate poorly with the results of DCG, especially for those patients with normal DCGs. On the basis of these data, syringing would not be a good substitute for DCG.

Alternatively, lacrimal scintigraphy would appear to be suitable. This technique was first described by Rossomondo et al (1972). Technetium-99m sulphur colloid eyedrops are administered and the activity within the lacrimal drainage system imaged to monitor the progress of tracer through the system. Scintigraphy is simple to perform and physiological, using the natural lacrimal drainage process to introduce the radiopharmaceutical into the system. It is a more sensitive test of obstruction than DCG, especially at common canalicular level (Amanat et al, 1979, 1983; Rose & Clayton, 1985). It can demonstrate the level of obstruction in the majority of cases (Amanat et al, 1979), but cannot distinguish medial from lateral canalicular block. In addition, it may show abnormality in those patients with epiphora due to eyelid laxity but patent drainage systems (Hurwitz & Victor, 1985). The dose of radiation to the ocular lens is much lower in scintigraphy than in DCG—a maximum of 20 mrad (20×10^{-5} Gy) in scintigraphy (Amanat et al, 1979) compared with a measured 1644 mrad (16×10^{-3} Gy) in subtraction macrodacryocystography (Galloway et al, 1984).

A number of conclusions can be drawn from this study. It is important to assess and counsel patients carefully before requesting DCG. In our patients, the presence, but not the level, of obstruction on a DCG was an important factor in determining whether a patient had lacrimal surgery. The level of obstruction did not influence the lacrimal surgery used. This suggests that any investigation which distinguishes patent from obstructed systems may be as useful as DCG. Lacrimal scintigraphy may provide sufficient information with less discomfort and radiation burden to the patient.

References

Amanat, L. A., Wraight, E. P., Watson, P. G. & Hawkins, T. D., 1979. Role of lacrimal scintigraphy and subtraction macrodacryocystography in the management of epiphora. *British Journal of Ophthalmology*, *63*, 511–519.

Amanat, L. A., Hilditch, T. E. & Kwok, C. S., 1983. Lacrimal scintigraphy II. Its role in the diagnosis of epiphora. *British Journal of Ophthalmology*, *67*, 720–728.

Campbell, W., 1964. The radiology of the lacrimal system. *British Journal of Radiology*, *37*, 1–26.

Chapman, S. & Nakielny, R., 1986. Dacryocystography. In *A Guide to Radiological Procedures* (Baillière Tindall, London), pp. 250–251.

Ewing, A. E., 1909. Roentgen ray demonstrations of the lacrimal abscess cavity. *American Journal of Ophthalmology*, *26*, 1–4.

Galloway, J. E., Kavic, T. A. & Raflo, G. T., 1984. Digital subtraction macrodacryocystography. A new method of lacrimal system imaging. *Ophthalmology*, *91*, 956–962.

Hurwitz, J. J. & Victor, W. H., 1985. The role of sophisticated radiological testing in the assessment and management of epiphora. *Ophthalmology*, *92*, 407–413.

Lloyd, G. A. S. & Welham, R. A. N., 1974. Subtraction macrodacryocystography. *British Journal of Radiology*, *47*, 379–382.

Rose, J. D. G. & Clayton, C. B., 1985. Scintigraphy and contrast radiography for epiphora. *British Journal of Radiology*, *58*, 1183–1186.

Rossomondo, R. M., Carlton, H., Trueblood, J. H. & Thomas, R. P., 1972. A new method of evaluating lacrimal drainage. *Archives of Ophthalmology (Chicago)*, *88*, 523–525.

Welham, R. A. N., 1987. The lacrimal drainage apparatus. In *Clinical Ophthalmology*, ed. by S. Miller (John Wright, Bristol), pp. 341–411.

1990, *The British Journal of Radiology*, *63*, 340–345

Oropharynx carcinoma: irradiation alone *versus* induction chemotherapy plus irradiation—5 year results

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Abstract. Induction chemotherapy (CT) has demonstrated overall response rates of 80% for oropharynx carcinomas, but no overall survival benefit has been reported. In order to determine the value of induction CT for such patients, we conducted a retrospective study: 121 patients were treated with CT and radiotherapy (RT) (Group 1). This group was compared with a historical group of 84 patients treated by RT alone (Group 2). The CT used was Cisplatinum associated with Bleomycin and Vincristin or Vindesin and with 5 Fluoro-uracil. An objective response to CT was observed for 41% of patients. The 5 year actuarial survival rate was 19% for Group 1 and 24% for Group 2. Patterns of failure were identical in the two groups. The only difference observed was for patients with N3 nodes (26% of 5 year survival rate in Group 1 *versus* 9% in Group 2) ($p = 0.05$). The results did not depend on the histological differentiation, the tumour site or the type of CT. We conclude that this retrospective study failed to demonstrate an advantage for induction CT in oropharynx carcinoma except for patients with N3 nodes.

Oropharynx carcinomas are known to have a poor prognosis. Patients with T1 or T2 tumours treated with surgery or radiation have a 5 year survival rate of about 70% (Fletcher, 1980; Perez et al, 1982; Million & Cassisi, 1984). However, applying the same treatment to patients with T3 or T4 tumours has given poor results. Locoregional evolution (relapse or progression) occurred in 50–60% of the patients, distant metastasis in 10–20% and secondary cancer in 10–25% (Fletcher, 1980; Million & Cassisi, 1984).

As a result, several authors have introduced chemotherapy in the treatment of these cancers, especially for patients with a high risk of local progression. Several drugs have been used alone or combined in the initial treatment of these upper aerodigestive tract tumours. The feasibility of these treatments has been demonstrated and objective response rates have been obtained in 30–80% of the patients, depending on the drug combination used (Tarplay et al, 1975; Elias et al, 1979; Wittes et al, 1979; Glick & Taylor, 1981). With a combination of Cisplatinum (CDDP) and 5 Fluoro-uracil (5FU), response rates over 80% have been reported. Responders seemed to have a higher survival rate than non-responders (Amrein & Weitzman, 1985; Rooney et al, 1985).

However, none of these studies indicated better long-term survival for these patients. Trials published on this subject have evaluated results for patients with head and neck carcinomas. The objective response rate depends strongly on the primary site of the tumour (Amer et al, 1979).

The objective of the present study was to evaluate the role of induction chemotherapy (before locoregional treatment) on the locoregional control and long-term survival of a homogenous group of patients with oropharynx carcinomas alone.

Materials and methods

Selection criteria

In order to evaluate the role of induction chemotherapy in the treatment of upper aerodigestive tract carcinomas, two groups of patients, as homogenous as possible according to the treatment received, were defined. Patients with a squamous cell carcinoma of the oropharynx, histologically proven and treated by irradiation alone were included. Patients with multiple tumours, or metastasis or treated with a palliative intent were excluded. All the patients were treated by the same medical team between 1978 and 1986.

Description of the population

Two hundred and five patients divided into two groups were evaluated for this study. In Group 1, 121 patients were treated by induction chemotherapy followed by radiotherapy. This group was compared with a historical group of 84 patients treated by irradiation alone (Group 2).

The mean age was 56.2 years in Group 1 and 57.3 years in Group 2. The performance status was scored according to the WHO scale (Miller et al, 1981), and it was similar in the two groups. Grade 0 or 1 was recorded for more than 90% of the patients.

The anatomical localization of the primary tumour was identical in the two groups. Two sites were preferentially represented: the tonsillar fossa and the base of the tongue.

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Table I. Patient characteristics

Characteristic	CT+RT	RT
No. of patients	121	84
Age (years)	56	57
Performance status		
0	81 (67%)	55 (65%)
1	30 (25%)	18 (21%)
2	9 (7%)	8 (10%)
3	1	3
4	0	0
Tumour site		
Tonsillar fossa	51 (42%)	39 (46%)
Soft palate	10 (8%)	9 (11%)
Base of tongue	49 (41%)	33 (39%)
Pharynx post wall	5	1
Others	6	2
Histological grading		
Well differentiated	63 (52%)	42 (50%)
Moderately diff.	37 (31%)	23 (27%)
Undifferentiated	13 (11%)	13 (15%)
Unknown	8	6

CT, chemotherapy; RT, radiotherapy.

Table III. Chemotherapy regimens used

Drugs						Patients	Cycles
CDDP	5FU	BLM	MTX	VCR	VDS		
×	×					18	3
×		×	×	×		27	2
×	×	×	×	×	×	1	2
×		×			×	64	2
×					×	1	2
		×	×	×		6	2
		×		×		3	2
×		×		×		1	2

CDDP, Cisplatinum; 5FU, 5 Fluoro-uracil; BLM, Bleomycin; MTX, Methotrexate; VCR, Vincristrin; VDS, Eldesin.

All the tumours were squamous cell carcinomas. The pathological grading was equally represented in the two groups studied (Table I). Patient distribution according to the TNM classification of 1979 (UICC, 1979) is shown in Table II. The main population included patients with T3 or T4 tumours (71% in Group 1 and 62% in Group 2). Patients with N3 lymph nodes were also widely represented: 43% in Group 1 and 40% in Group 2.

Treatment methods

All the patients were treated either by chemotherapy and radiotherapy or by radiotherapy alone.

Chemotherapy. According to the data for drug combinations in the literature, several protocols were utilized in this study (Table III). Three main combinations were applied.

From July 1978 to January 1981, 27 patients received: CDDP 25 mg/m^2/day from D1 to D4; Bleomycin (BLM) 15 mg/m^2/day from D1 to D4; Vincristin (VCR) 2 mg/m^2 on D1; Amethopterin (MTX) 30 mg/m^2 on D4. Two cycles were given with a 3 week interval.

From January 1981 to July 1985, 64 patients received: CDDP 25 mg/m^2 from D1 to D4; BLM 15 mg/m^2/day from D1 to D4; Eldisin (VDS) 3 mg/m^2/day on D1. Two cycles were given with a 3 week interval.

Since July 1985, 18 patients received: CDDP 120 mg/m^2 on D2; 5FU 1 g/m^2 in continuous infusion from D1 to D5. Three cycles were given with this regimen with a 3 week interval.

During the chemotherapy all the patients received corticosteroids (Methylprednisolone at doses of about 80 mg/day) for 4–5 days and also metoclopramid to combat nausea.

Table II. Patient population by tumour and nodal class[a]

Nodal status	Tumour size				
	T1	T2	T3	T4	TX
Chemotherapy and radiotherapy					
N0	0	12	24	2	0
N1	0	2	11	1	0
N2	0	0	5	1	0
N3	2	8	34	8	0
NX	0	0	0	0	11
Radiotherapy alone					
N0	4	9	18	4	0
N1	1	1	5	0	0
N2	0	1	1	0	0
N3	2	8	20	4	0
NX	0	0	0	0	6

[a] TNM UICC 1979 classification. T, tumour; N, node.

Radiotherapy. External radiotherapy alone was the most widely used treatment technique (119/121 in Group 1 and 78/84 in Group 2). Brachytherapy was also used in eight cases (two in Group 1 and six in Group 2).

External radiotherapy was performed with a cobalt-60 unit, the patient lying on his back. The primary tumour and the upper neck were treated with two parallel opposed portals to the subdigastric area, and the lower neck with an anterior portal shielding the larynx. All patients received 1.8–2.25 Gy/fraction four to five times a week. The mean total tumour dose was 69 Gy in Group 1 and 71 Gy in Group 2. The dose delivered to the lower neck was 45 Gy for N0 patients and 55 Gy in the homolateral lower neck for patients with palpable nodes in the upper neck.

Evaluation methods

Clinical analysis. Clinical examination was performed before beginning the treatment and after completing the chemotherapy. Tumour extension was classified during a multidisciplinary examination according to the TNM classification (UICC, 1979). Tumour regression obtained with chemotherapy was evaluated according

Table IV. Response to chemotherapy

Response	CDDP+VCR +BLM+MTX	CDDP+VDS +BLM	CDDP +5FU
Complete (CR)	0	6 (9%)	2 (11%)
Partial (PR)	10 (37%)	20 (32%)	8 (45%)
No response (NR)	17 (63%)	38 (60%)	8 (45%)
CR+PR	10 (37%)	26 (41%)	10 (56%)

CDDP, Cisplatinum; VCR, Vincristin; BLM, Bleomycin; VDS, Vindesin; 5FU, 5 Fluoro-uracil.

Table V. Patterns of failure

Pattern of failure	G1		G2	
	n	%	*n*	%
Tumour persistence	41	34	19	23
Loco-regional relapse	28	23	18	21
Distant metastases (DM)	8	6	8	9
Tumour persistence+DM	3		1	
Loco-regional relapse+DM	5		1	
Secondary cancer	8	7	7	8
Intercurrent disease	8	7	8	9

G1, Chemotherapy+radiotherapy; G2, radiotherapy alone.

the criteria of WHO (Miller et al, 1981). The response was considered as complete when the tumour clinically disappeared, partial when the tumour volume shrinkage was equal to 50% or above, and absent when the regression was under 50%. Only patients with a complete or partial response to the treatment were considered as responders. The clinical response was evaluated 6 weeks after the end of the radiation therapy. Immediate locoregional control was scored when no tumour was visible during this clinical evaluation. The tolerance to chemotherapy and radiotherapy was analysed according to the WHO scale of acute clinical and biological side effects.

Statistical analysis. Survival rates were calculated according to the actuarial method. If a difference was found between two groups the significance was analysed using the Logrank test.

Results

Overall response rate to induction chemotherapy was analysed in 120 patients. An objective response was obtained for 41% of the patients (49/120) with 7% of complete response (9/120). With the drug regimen associating CDDP+BLM+VCR+MTX there was a 37% response rate, 41% with the combination of CDDP, BLM and VDS and 56% with CDDP and 5FU (Table IV). The difference was not statistically significant. Overall actuarial survival at 3 years and 5 years was respectively 27% and 19% for Group 1 and 32% and 24% for Group 2 (Fig. 1).

Locoregional control at 5 years was 36% in Group 1 and 45% in Group 2. The main cause of failure for the two groups was locoregional progression and relapse; the other causes of failure were distant metastasis and secondary cancer (Table V).

We then tried to find out if there was a group of patients whose long-term overall survival was increased by chemotherapy. For this reason the results obtained with the two treatment modalities were analysed separately for all the tumour parameters (anatomical site, tumour bulk, nodal status and pathological grading).

The overall actuarial survival was similar for patients of the two groups with the same anatomical tumour site. Patients with a tumour in the tonsillar region achieved a 26% 5 year survival rate with induction chemotherapy and 16% without chemotherapy (Fig. 2). For cancers of the base of the tongue, rates were respectively 13% and 18% with or without chemotherapy (Fig. 3).

The results obtained for patients with a similar tumour bulk according to the TNM classification were

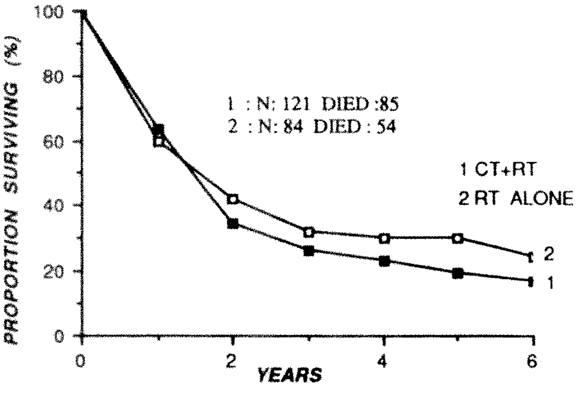

Figure 1. Actuarial overall survival in the two groups (chemotherapy plus irradiation *versus* irradiation alone). No difference in survival is noted between the two groups.

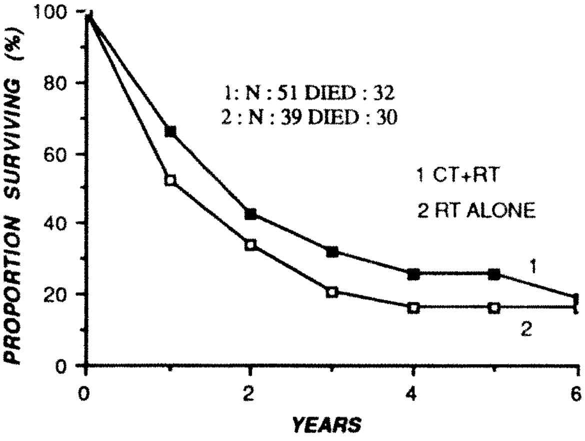

Figure 2. Actuarial survival for tonsillar fossa primary tumour.

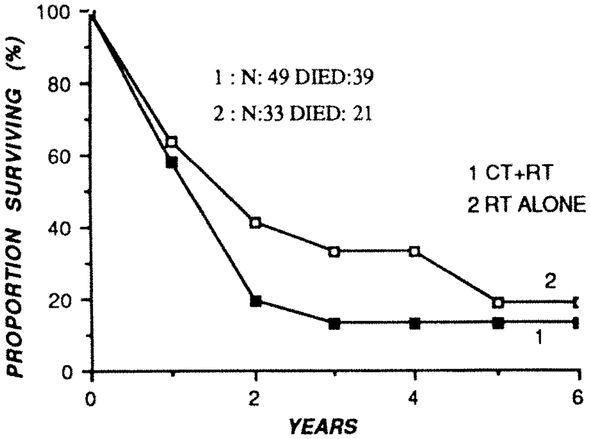

Figure 3. Actuarial survival for primary tumours on the base of the tongue. No difference is noted between these results and those of Fig. 2.

analysed. The 5 year overall survival for T1 and T2 was 55% with chemotherapy and radiotherapy and 57% with radiotherapy alone.

In larger tumours (T3 and T4), overall survival according to treatment modalities was respectively 18% and 13% (Fig. 4). Only one group of patients with N3 lymph nodes appeared to benefit from chemotherapy. For these patients the survival rate with a combined treatment modality was 26% against 9% with radiotherapy alone ($p = 0.05$) (Fig. 5).

When the pathological gradings scored on the biopsy were identical the same results were obtained with the two treatment modalities. It should be pointed out that for patients with a low grade tumour or an undifferentiated tumour the actuarial 5 year survival was 20% for Group 1 and 0% for Group 2. Because of the small number of patients, 13 in each group, the difference was not statistically significant.

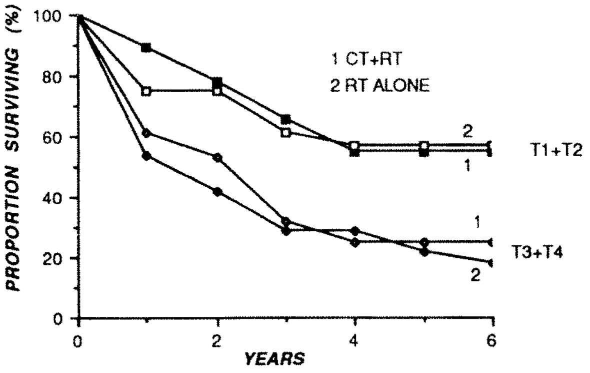

Figure 4. Actuarial survival in the two therapeutic groups when the tumour bulk is similar. Tumour bulk is a prognostic factor but when the tumour bulk is similar there is no difference between the two groups.

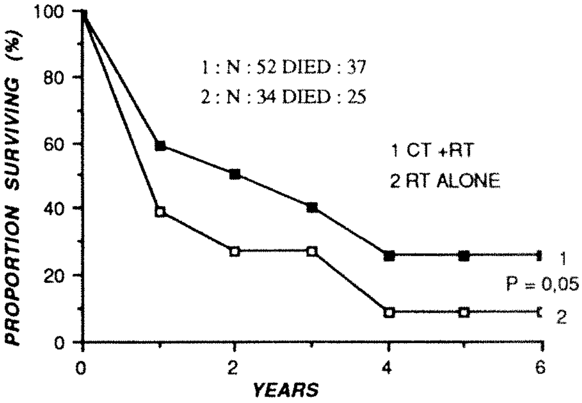

Figure 5. Actuarial survival for N3 patients. In this group there is a difference ($p = 0.05$) in favour of the chemotherapy group.

There was no difference in the survival rate of patients treated with one of the three main drug combinations associated with radiotherapy and no difference when compared with patients receiving radiotherapy alone. However, only 18 patients were treated with CDDP and 5FU followed by irradiation.

In Group 1 the survival rate of responders to chemotherapy was 36% *versus* 11% for non-responders ($p = 0.03$), as has been observed in other studies.

Tolerance to treatment

The tolerance to chemotherapy was generally good: 80% of patients suffered from nausea and vomiting. These side effects were quoted grade 3 or 4 in 10% of patients. Haematological toxicity occurred in 15% of patients and resulted in a reduction of the drug dose or an increase in the time interval between the two cycles. Transient renal function impairment occurred in four patients, who recovered when the CDDP administration was stopped. Pneumonopathy secondary to BLM was observed in one case and for eight patients peripheral neuropathy symptoms were noted.

The immediate tolerance to irradiation was similar in the two groups. Oral mucositis grade 3 or 4 was noted in 17% of Group 1 patients and in 21% of Group 2 patients.

Complications

Late serious complications occurred in 15 cases (nine in Group 1, six in Group 2). Eight patients had bone necrosis with two requiring a partial mandibulectomy (five were in Group 1 and three in Group 2). Three patients had soft tissue necrosis (two in Group 1 and one in Group 2). Four patients had a severe trismus (two in Group 1 and two in Group 2). Fifteen per cent of the Group 1 patients had a cervical oedema *versus* 11% in Group 2.

No difference was observed between the two groups in terms of late complications.

Discussion

The data obtained show that the long-term overall survival of patients with squamous cell carcinoma of the oropharynx was not improved by induction chemotherapy preceding radiotherapy. These results were not dependent upon the chemotherapy regimen or on the anatomical site, the pathological grading or the bulk of the tumour. Only patients with N3 lymph nodes treated by induction chemotherapy followed by radiotherapy had a statistically better overall survival rate than patients receiving radiotherapy alone.

This study was conducted over a long time period and three major protocols of chemotherapy were used. With the first two combinations only 35–40% of patients had objective responses, and it should be asked whether the optimal chemotherapy protocol was tested. Overall response rates around 90% with more than 50% of complete responses were reported with other drug combinations (Kies et al, 1984; Weaver et al, 1984; Amrein & Weitzman, 1985; Rooney et al, 1985). However, the survival rate was not improved in controlled trials with these protocols, even though there was a high overall response rate (Schuller et al, 1983; Holoye et al, 1985).

The results of the present study do not show that induction chemotherapy improved the long-term survival. These data are not different from those observed in other studies or in controlled trials including more heterogenous groups of patients with any type of upper aerodigestive tract tumour (Vogl et al, 1982; Schuller et al, 1983; Cripps et al, 1985; Holoye et al, 1985). In the group of patients studied, even though the tumour site was very homogenous, analysis of reasons for failure in each of the two therapeutic groups gave the same results.

In this study, induction chemotherapy did not decrease the frequency of occurrence of distant metastasis as has been reported by others (Slotman et al, 1984; Hong et al, 1985). Nevertheless, it seems that maintenance chemotherapy after locoregional treatment can lead to significantly decreased rates of distant metastasis (Slotman et al, 1984; Hong et al, 1985). But it is quite difficult to maintain such a treatment in patients with upper aerodigestive tract cancers (Head and Neck Contract Program, 1987).

Analysis of results observed in the different subgroups with one of two therapeutic regimens did not show any difference.

Only the group of patients with N3 lymph nodes seemed to benefit from induction chemotherapy. Still, these results must be viewed with caution because the numbers of patients are small and the study is retrospective. Parameters such as anatomical site, pathological grading and tumour bulk did not influence the results obtained with induction chemotherapy.

It seems that even if induction chemotherapy does not dramatically improve the overall survival level it could play a role in providing a better quality of life. Indeed, should major surgery (pelvi-mandibulectomy or transmaxillary bucco-pharyngectomy) be proposed, induction chemotherapy could be tried first to allow more conservative treatment with radiotherapy where there is a favourable response.

In conclusion, induction chemotherapy should not be automatically proposed for patients with upper aerodigestive tract carcinomas. It is necessary to perform new controlled trials with drug regimens yielding a high response rate, especially complete responses, to determine more accurately the respective roles of induction chemotherapy and maintenance chemotherapy.

Acknowledgment

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References

AMER, M. H., AL SARRAF, M. & VAITKEVICIUS, V. F., 1979. Factors that affect the response to chemotherapy and survival of patients with advanced head and neck cancer. *Cancer, 43*, 2202–2206.

AMREIN, P. C. & WEITZMAN, S. A., 1985. Treatment of squamous cell carcinoma of the head and neck with Cisplatin and 5 Fluoro-uracil. *Journal of Clinical Oncology, 3*, 1632–1639.

CRIPPS, C., ODELL, P. & DANJOUX, C., 1985. Pretreatment with chemotherapy in patients with advanced head neck cancer. *Journal of Otolaryngology, 25*, 391–393.

ELIAS, E. G., CHRETIEN, P. B., MONNARD, E., KHAN, T., BOUCHELLE, W. H., WIERNICK, P. H., LIPSON, S. D., HANDE, K. R. & ZANTAI, T., 1979. Chemotherapy prior to local therapy in advanced squamous cell carcinoma of the head and neck: preliminary assessment of an intensive drug regimen. *Cancer, 43*, 1025–1031.

FLETCHER, G. H., 1980. *Textbook of Radiotherapy*, 3rd edn. (Lea and Febiger, Philadelphia), p. 286.

GLICK, J. H. & TAYLOR, S. G., 1981. Integration of chemotherapy into a combined modality treatment plan for head and neck cancer: a review. *International Journal of Radiation Oncology, Biology, Physics, 7*, 229–242.

HEAD AND NECK CONTRACT PROGRAM, 1987. Final report: adjuvant chemotherapy for advanced head and neck squamous carcinoma. *Cancer, 60*, 301–311.

HOLOYE, P. Y., GROSSMAN, T. W. & TOOHIL, R. J., 1985. Randomized study of adjuvant chemotherapy for head and neck cancer. *Otolaryngology and Head and Neck Surgery, 93*, 712–717.

HONG, W. K., BROMER, R. H., AMATO, D. A., SHAPSHAY, S., VINCENT, M., VAUGHAN, C., WILLET, B., KATZ, A., WELCH, J., FOFONOFF, S. & STRONG, S., 1985. Locally advanced head and neck cancer patients who achieved complete remission after combined modality therapy. *Cancer, 56*, 1242–1245.

KIES, M. S., PECARO, B. C. & GORDON, L. J., 1984. Preoperative combination chemotherapy for advanced stage head and neck cancer. *American Journal of Surgery, 148*, 367–371.

MILLER, A. B., HOOGSTRATEN, B., STAQUET, M. & WINKLER, A., 1981. Reporting results of cancer treatment. *Cancer, 47*, 207–214.

MILLION, R. R. & CASSISI, N. J., 1984. Oropharynx. In *Management of Head and Neck Cancer. A Multidisciplinary Approach*, ed. by R. R. Million & N. J. Cassisi (J. B. Lipincott, Philadelphia), p. 299.

PEREZ, C. A., PURDY, J. A. & BREAUX, S. R., 1982. Carcinoma of the tonsillar fossa. A non randomized comparison of preoperative radiation and surgery or irradiation alone: long term results. *Cancer, 50*, 2314–2318.

Rooney, L., Kish, J., Jacobs, J., Kinzie, J., Weaver, A., Crissman, J. & Al Sarraf, M., 1985. Improved complete response rate and survival in advanced head and neck cancer after three course induction therapy with 120 hour 5FU infusion and Cisplatin. *Cancer, 55*, 1123–1128.

Schuller, D. E., Wilson, H. E., Smith, R. E. Batley, F. & James, A. D., 1983. Preoperative reductive chemotherapy for locally advanced carcinoma of the oral cavity, oropharynx and hypopharynx. *Cancer, 51*, 15–19.

Slotman, G. T., Mohit, T., Raina, S., Swaminathan, A. P., Ohanian, M. & Rush, B. F., 1984. The incidence of metastases after multimodal therapy for cancer of the head and neck. *Cancer, 54*, 2009–2014.

Tarplay, J. L., Chretien, P. B. & Alexander, J. C., 1975. High dose methotrexate as a preoperative adjuvant in the treatment of epidermoid carcinoma of the head and neck: a feasibility study and clinical trial? *American Journal of Surgery, 130*, 481–486.

UICC, 1979. *TNM Classification of Malignant Tumors*, 3rd edn (International Union against Cancer, Geneva).

Vogl, S. E., Lerner, H. & Kaplan, B. H., 1982. Failure of effective initial chemotherapy to modify the course of stage IV (MO) squamous cancer of the head and neck. *Cancer, 50*, 840–844.

Weaver, A., Fleming, S. & Ensley, J., 1984. Superior clinical response and survival rates with initial bolus of Cisplatin and 120 hours infusion of 5 Fluoro-uracil before definitive therapy for locally advanced head and neck cancer. *American Journal of Surgery, 148*, 525–529.

Wittes, R., Heller, K. & Randolph, V., 1979. Cis-dichlorodiamine-planitum based chemotherapy as initial treatment of advanced head and neck cancer. *Cancer Treatment Report, 63*, 1533–1538.

1990, *The British Journal of Radiology*, 63, 346–348

Silicone implant to prevent visceral damage during adjuvant radiotherapy for retroperitoneal sarcoma

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Abstract. The incidence of local recurrence after surgery for retroperitoneal sarcoma is reduced by high-dose adjuvant radiotherapy but treatment is restricted by the effects of irradiation on adjacent viscera. By securing a silicone gel-filled implant (breast prosthesis) in the tumour bed after excision of the tumour, adjacent viscera are displaced from the site of maximum irradiation and may thereby be protected. We used this technique in three patients in whom excision of a retroperitoneal sarcoma was followed by high-dose adjuvant radiotherapy. Post-operative radiotherapy was well tolerated but local recurrence developed in one patient, and delayed perforation of the large bowel occurred in another. Both cases underwent further surgery at which the implant was removed. The same two cases also developed asymptomatic hydronephrosis on the side of the implant, attributed to local fibrosis.

Sarcomas of the retroperitoneum account for around 12% of all soft tissue tumours (Lawrence et al, 1987). The commonest types are liposarcoma and leiomyosarcoma (Stower & Hardcastle, 1982). Because of their position, complete surgical excision is technically possible in only about 50% of cases (Cody et al, 1981; McGrath et al, 1984) and even then local recurrence is common (Cody et al, 1981; Stower & Hardcastle, 1982). The 5 year disease-free survival rate after complete excision is less than 60% and falls to below 10% when excision is incomplete (Cody et al, 1981; Storm et al, 1981).

Adjuvant radiotherapy reduces local recurrence and improves survival (Cody et al, 1981; Tepper et al, 1984) but it is limited by the effects of irradiation on adjacent organs, of which radiation enteritis is the most serious (Kinsella et al, 1988).

We report three cases of retroperitoneal sarcoma in which a silicone gel-filled breast prosthesis was secured in the tumour bed after excision of the primary tumour in order to displace adjacent viscera prior to adjuvant radiotherapy. Computed tomography (CT) was used post-operatively to plan treatment.

Patients and methods

Case 1

A 47-year-old woman presented with lumbar backpain which she had had for 3 months. Computed tomographic examination showed a retroperitoneal mass in the left loin. At laparotomy an 8 × 5 × 4 cm retroperitoneal tumour attached to the diaphragm, quadratus lumborum and 11th rib was excised with adjacent muscle and periosteum. Under antibiotic cover, a 205 c.c. silicone implant was placed in the tumour bed, which was marked with titanium clips. The prosthesis was supported in an omental sling based on the right gastroepiploic artery and peritoneum was closed over it. The diaphragm was repaired over a chest drain. Histology showed the tumour to be a malignant fibrous histiocytoma. Three weeks post-operatively the patient received external beam radiotherapy (EBRT) delivered with the patient prone using a CT planning facility; 50 Gy were given in 25 fractions by an isocentric technique using anterior and posterior oblique fields 17.5 × 7 cm in size, followed by 10 Gy given in 5 fractions to the posterior abdominal wall using 10 MeV electrons given by direct field. The total dose to the site of excision was 58 Gy in 30 fractions. Treatment was well tolerated with no nausea or diarrhoea and the patient is well without gastrointestinal symptoms or evidence of recurrent tumour 12 months following treatment.

Case 2

A 56-year-old man presented with a large mass in the left iliac fossa. Computed tomographic examination showed a retroperitoneal tumour lying on the left psoas muscle and common iliac vessels, displacing the ureter and causing hydronephrosis. At laparotomy a 13 × 12 × 8 cm tumour was found lying behind the left colon, The colon was reflected and the tumour excised with part of the psoas muscle. Under antibiotic cover, a 400 c.c. silicone implant was placed in the tumour bed, which was marked with titanium clips, and covered with peritoneum. Histology revealed a myxoid liposarcoma. Post-operative EBRT was delivered with the patient supine using a CT planning facility (Figs 1 and 2). A modal dose of 50 Gy in 25 fractions was given by an isocentric technique using right anterior, right lateral oblique and left posterior oblique fields. A further 10 Gy

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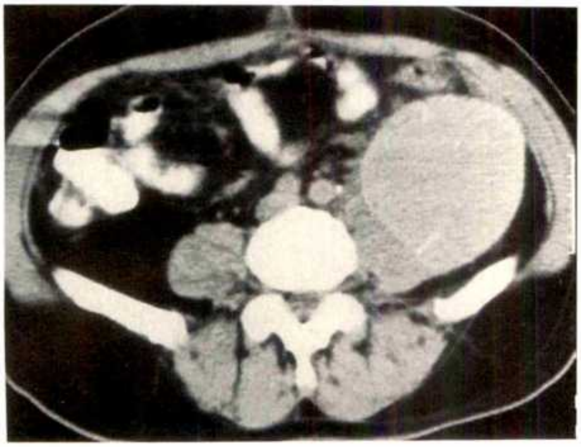

Figure 1. Computed tomographic scan of Case 2 showing silicone implant in tumour bed.

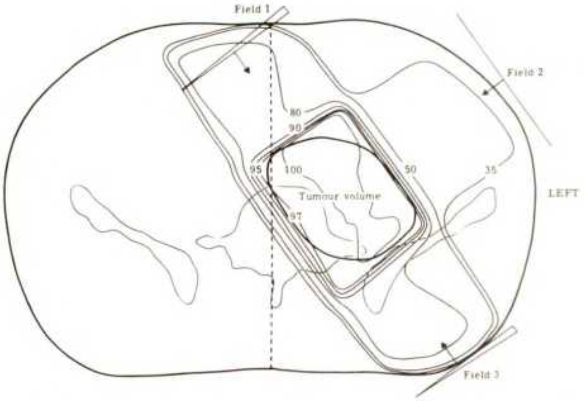

Figure 2. Treatment plan for Case 2 showing irradiation fields and isodose profiles.

in 5 fractions were administered to a reduced volume by the same technique. One month after surgery the patient was admitted with fever and left iliac fossa pain. A precise cause was not established but the condition resolved in 48 h with broad spectrum antibiotics. A CT scan performed 4 months later demonstrated left hydronephrosis but no evidence of local recurrence, and intravenous urogram showed delayed excretion of contrast medium by the left kidney. After a further 13 months the patient presented again with fever and left iliac fossa pain. A repeat CT scan showed a fluid collection around the spacer. Laparotomy revealed a faeco-purulent collection in a fibrous cavity which contained the implant and communicated with the left colon. No recurrent tumour was seen. The implant was removed, the cavity drained, and a temporary defunctioning transverse colostomy was created. The patient has made a satisfactory recovery.

Case 3

A 56-year-old woman, who had originally undergone excision of a retroperitoneal sarcoma lateral to the sigmoid colon, developed recurrent tumour 2 years later which was excised with adjacent bowel. After 11 months a second recurrence developed and the patient presented with pain and a firm ballotable mass in the left flank. The recurrent tumour was resected *en-bloc* with sigmoid colon and a large bowel anastomosis was performed. The lower pole of the left kidney was drawn forwards and secured to the anterior abdominal wall. Six plastic afterloading catheters were inserted into the tumour bed and a 340 c.c. silicone implant was folded into an omental pocket and fixed to the psoas fascia to displace the colonic anastomosis and small bowel medially. The tumour was identified as a malignant peripheral nerve sheath tumour. Eight days after operation, the catheters were loaded with irridium wires, 14.5–17.5 cm long, and 20 Gy administered to the 85% reference point over 47 hours. Two weeks later, EBRT was commenced with anterior and posterior parallel-opposed fields to a total midpoint dose of 50 Gy in 25 fractions using 5 MeV photons. Although treatment was well tolerated with no nausea or vomiting, the patient complained of postprandial left sided abdominal pain and developed induration of the flank. Ten months after completion of treatment, a CT examination showed left hydronephrosis and a small nodule overlying the left iliac vessels. At laparotomy a 3 × 3 × 2 cm recurrence was found just below the prosthesis but not involving the ureter. Hydronephrosis was attributed to extensive local fibrosis. The prosthesis was removed with the recurrent tumour and the patient remains well 5 months later with no evidence of further recurrence.

Discussion

Complications from radiation enteritis occur when the total dose of irradiation delivered to the abdomen exceeds 45 Gy (Galland & Spencer, 1987). They include spontaneous perforation of the bowel, anastomotic dehiscence, and the late development of strictures and fistulae (Glenn et al, 1985). The total dose of irradiation used for adjuvant treatment of retroperitoneal sarcoma is at least 45 Gy and even higher doses achieve better local control (Tepper et al, 1984). However, the risk of complications increases with the dose of radiation.

There is little evidence that pharmacological agents prevent radiation damage effectively (Galland & Spencer, 1987) and, while adjacent tissues are spared to some extent by using intraoperative radiotherapy (IORT) (Kinsella et al, 1988), the technique is cumbersome and requires elaborate resources.

In cases with pelvic malignancy the small bowel can be temporarily excluded from the radiation field by employing the Trendelenberg position or distending the bladder before treatment (Green et al, 1983). It can also be displaced by surgical means using an omental sling or an artificial pelvic diaphragm made from adjacent tissues or synthetic materials (Galland & Spencer, 1987).

Yet another approach has been described whereby an artificial "spacer" is used to plug the pelvis after pelvic exenteration (Durig et al, 1984). A silicone breast prosthesis has been recommended for this purpose because it is simple to insert and does not require removal in the absence of complications (Sugarbaker, 1983).

We adapted this technique for patients undergoing excision of retroperitoneal sarcoma in whom high-dose post-operative irradiation was planned. The prosthesis was held in place by peritoneum or omentum and the tumour bed marked with titanium clips to avoid radiological artefacts during CT planning.

Post-operative radiotherapy was well tolerated in all three patients.

One patient (Case 3) developed local recurrence despite high-dose irradiation. However, this patient had a malignant peripheral nerve sheath tumour which has the reputation of being radioresistant (Lindberg et al, 1981).

Two patients developed asymptomatic hydronephrosis on the side of the implant. Both subsequently underwent laparotomy which revealed extensive fibrosis at the lower end of the ureter, attributed to irradiation.

The most serious complication was delayed perforation of the colon (Case 2). This may have been a result either of chronic infection of the implant or of a late effect of high-dose radiotherapy, although another patient (Case 3) who received an even higher total dose of irradiation has so far developed no bowel complications despite the presence of a surgical anastomosis.

The three cases illustrate the difficulty of protecting the abdominal viscera while delivery a high-dose of irradiation to the site of potential residual tumour. Local recurrence is probably inevitable with certain aggressive soft tissue tumours but perforation of the bowel is clearly an unacceptable complication of treatment. Perforation might have been avoided, if chronic infection had been confirmed, by removal of the prosthesis at an earlier stage, but we have been reluctant to advise its elective removal in the absence of complications as this would inflict further surgery on a patient whose prognosis is already unfavourable. A possible compromise would be to use either an expandable prosthesis that could be withdrawn following radiotherapy in the same way as an abdominal drain, or a prosthesis made entirely from absorbable material.

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References

Cody, H. S., Turnbull, A. O., Fortner, J. G. & Hadju, S. I., 1981. The continuing challenge of retroperitoneal sarcomas. *Cancer, 47*, 2147–2152.

Durig, M., Steenblock, U. & Herberer, M., 1984. Prevention of radiation injuries to the small intestine. *Surgery Gynecology and Obstetrics, 159*, 162–163.

Galland, R. B. & Spencer, J., 1987. Natural history and surgical management of radiation enteritis. *British Journal of Surgery, 74*, 742–747.

Glenn, J., Sindelar, W. F., Kinsella, T., Glatstein, E., Tapper, J., Costa, J., Baker, A., Sugarbaker, P., Brennan, M. F., Seipp, C., Wesley, R., Young, R. C. & Rosenberg, S. A., 1985. Results of multimodality therapy of resectable soft-tissue sarcomas of the retroperitoneum. *Surgery, 97*, 316–324.

Green, N., Iba, G. & Smith, W. R., 1983. Measures to minimize small intestinal injury in the irradiated pelvis. *International Journal of Radiation Oncology, Biology, Physics, 9*, 1385–1390.

Kinsella, T. J., Sindelar, W. F., Lack, E., Glatstein, E. & Rosenberg, S. A., 1988. Preliminary results of a randomized study of adjuvant radiation therapy in resectable adult retroperitoneal soft tissue sarcomas. *Journal of Clinical Oncology, 6*, 18–25.

Lawrence, W., Donegan, W. L., Natarajan, N., Mettlin, C., Beart, R. & Winchester, D., 1987. Adult soft tissue sarcomas: a pattern of care survey of the American College of Surgeons. *Annals of Surgery, 205*, 349–359.

Lindberg, R. D., Martin, R. G., Rohmsdahl, M. M. & Barkley, H. T., 1981. Conservative surgery and postoperative radiotherapy in 300 adults with soft-tissue sarcomas. *Cancer, 47*, 2391–2397.

McGrath, P. C., Neifeld, J. P., Lawrence, W., DeMay, R. M., Kay, S., Horsley, J. S. & Parker, G. A., 1984. Improved survival following complete excision of retroperitoneal sarcomas. *Annals of Surgery, 200*, 200–204.

Storm, F. K., Eilber, F. R., Mirra, J. & Morton, D. L., 1981. Retroperitoneal sarcomas. A re-appraisal of treatment. *Journal of Surgical Oncology, 17*, 1–7.

Stower, M. J. & Hardcastle, J. D., 1982. Malignant retroperitoneal sarcoma. A review of 32 cases. *Clinical Oncology, 8*, 257–263.

Sugarbaker, P. H., 1983. Intrapelvic prosthesis to prevent injury of the small intestine with high dosage pelvic irradiation. *Surgery Gynecology and Obstetrics, 157*, 269–271.

Tepper, J. E., Suit, H. D., Wood, W. C., Proppe, K. H., Harmon, D. & McNulty, P., 1984. Radiation therapy of retroperitoneal soft tissue sarcomas. *International Journal of Radiation Oncology, Biology, Physics, 10*, 825–830.

1990, *The British Journal of Radiology*, *63*, 349–354

The effect of Captopril on benign and malignant reactions in irradiated rat skin

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Abstract. The effect of the angiotensin converting enzyme inhibitor Captopril on the severity of radiation-induced epilation and moist desquamation and the incidence of skin tumours was determined for up to 52 weeks in male rats. The irradiation consisted of a range of single doses (0, 10, 20, 30 Gy) of ^{60}Co gamma rays to a 3.5 cm^2 right hemithorax port. Half of each radiation dose group consumed control powdered chow, and half consumed chow containing Captopril (50 mg/kg/day) continuously after irradiation. There were time- and radiation-dose-dependent increases in all three skin reactions. Rats exposed to 10 Gy exhibited a mild and transient epilation, but no moist desquamation or neoplasia in the radiation port. In animals exposed to 30 Gy, however, epilation began at 2 weeks after irradiation, reached a peak at approximately 7 weeks, then persisted essentially unchanged through 52 weeks. Captopril had no significant effect on the epilation reaction. Two waves of moist desquamation were observed after 30 Gy. The first appeared at 3 weeks after irradiation, reached a peak from 6–10 weeks, then subsided partially but significantly from 12–26 weeks. The second wave of moist desquamation began at 26–28 weeks, often was ulcerative, and occasionally was accompanied by the appearance of tumours in the irradiated volume. Captopril significantly ($p < 0.05$) reduced the severity of both phases of the moist desquamation reaction after 30 Gy, and reduced the percentage of animals exhibiting the most severe desquamation score (involving 50% of the radiation port). Of particular interest was the observation that Captopril also reduced the incidence of tumours. Of the 14 tumours detected, all were malignant (fibrosarcomas, squamous cell carcinomas), and only three ($p < 0.05$) occurred in rats receiving Captopril. Multiple tumours (three cases), tumours induced by 20 Gy (three cases), and tumours appearing before 6 months (one case) were observed only in rats consuming control diet, never in Captopril-treated animals. Animals which developed tumours in the second 6 months post-irradiation exhibited significantly more severe moist desquamation during the first 6 months than did the tumour-free members of their treatment group. Thus Captopril, known to ameliorate acute lung damage in irradiated rats, also reduces chronic benign and malignant skin reactions in the radiation treatment field.

Epilation, desquamation and tumour formation are untoward sequelae of radiation injury in skin. In the present study we determined the severity and incidence of these reactions in rat skin with respect to the effects of radiation dose and time post-exposure. We also evaluated the effect of the angiotensin converting enzyme (ACE) inhibitor Captopril on the pathogenesis of these radiation-induced skin lesions. Captopril (D-2-methyl-3-mercaptopropanoyl-L-proline) is used clinically in the management of systemic hypertension and congestive heart failure (Franciosa, 1987; Gavras & Gavras, 1987). Captopril also reduces radiation nephropathy in pigs (Robbins & Hopewell, 1986), and spares radiation-induced pulmonary endothelial dysfunction in rats (Ward & Hinz, 1987; Ward et al, 1988). In these experimental studies Captopril was administered after irradiation, thereby precluding possible action as a classic thiol radioprotector. Although the mechanism of therapeutic efficacy is not clear at present, these data suggest a novel and potentially important clinical application for Captopril as a modifier of radiation reactions in normal tissues. Of particular interest is the evidence that Captopril's ability to reduce radiation pathophysiology is neither species-specific nor tissue-specific. In the present study we determined whether Captopril (50 mg/kg/day, p.o.) could ameliorate radiation-induced skin reactions in rats examined up to 52 weeks after a range of single doses (0–30 Gy) of ^{60}Co γ rays.

Materials and methods

Male Sprague–Dawley rats (Charles River, Boston, MA) were housed at 23 ± 1°C, and were given powdered chow (Ralston Purina, St. Louis, MO) and tap water *ad libitum*. The drinking water contained 500 mg of oxytetracycline (Sigma Chemical Co., St. Louis, MO) per litre in order to prevent outbreaks of respiratory infections. All animals were housed in and cared for by the staff of the AAALAC-accredited Northwestern University Center for Experimental Animal Resources, in accord with NIH guidelines on the humane use of warm-blooded animals in research.

Rats weighing 350–400 g were anaesthetized with sodium pentobarbital (30 mg/kg, i.p.), and were exposed to single doses (10, 20, 30Gy) of ^{60}Co γ rays to a 3.5 cm^2 right hemithorax port as described previously (Ward et

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al, 1987). The dose rate was approximately 2.0 Gy/min. A staggered stack of 8 mm-thick paraffin blocks was placed adjacent to the right thorax, in order to eliminate the air space between the block tray and the treatment table within the port. Comparably handled sham-irradiated rats served as controls. Half of each radiation dose group consumed control powdered chow, and half consumed chow containing 0.08% (w/w) Captopril (E. R. Squibb, Princeton, NJ) continuously after irradiation. The control and experimental diets were available immediately after irradiation, although irradiated animals did not consume much feed in the first 24 h after anaesthesia (irradiation). Food consumption was measured periodically, and remained fairly constant at 25 ± 2 g/rat/day in all treatment groups throughout the study. This resulted in an average daily Captopril consumption of 20 mg/rat, a dose that was not adjusted for body weight gain. Thus the Captopril regimen decreased from 50 mg/kg/day to 25 mg/kg/day as the animals increased in body weight by a factor of approximately 2.0 during the 52 week study.

Animals were observed daily for the presence of tumours. Body weight, epilation, and moist desquamation were recorded weekly for the first 8 weeks, then biweekly for 52 weeks after irradiation. All treatment groups consisted initially of 32 rats, with eight animals per group scheduled for autopsy at 13, 26, 39 and 52 weeks after irradiation in order to evaluate pulmonary reactions.

Epilation in the port was scored on a scale of 0 = none, 1.0 = slight, 2.0 = moderate, 3.0 = severe and 4.0 = total, by two investigators unfamiliar with the treatment history of the animal. Moist desquamation was scored concurrently on a scale of 0 = none, 1.0 = skin surface intact but irregular, 2.0 = one to a few scattered foci of desquamation, 3.0 = confluent, but involving less than half of the port and 4.0 = involving more than half of the port. Tumour masses were fixed in 10% neutral buffered formalin at autopsy, sectioned at 6 μm, stained with hematoxylin and eosin, number coded, and evaluated by a veterinary pathologist.

All data were subjected to multiple analysis of variance, in order to assess the significance of the three controlled variables (time, radiation dose and diet). Scores for epilation and moist desquamation were obtained at each observation time as the arithmetic mean from all members of the treatment group. The significance of differences between group means was determined by the Neuman–Keuls test. Tumour incidence was evaluated by χ^2 analysis (Zar, 1974). All values represent the mean ± SEM.

Results

Most of the rats consuming control diet became extremely obese after 6 months of *ad libitum* access to powdered food; several had exceeded 900 g body weight by 9 months. Captopril-treated rats consumed approximately 10% less food and gained approximately 15% less body weight than did control-fed animals throughout the study (data not shown). In all other respects, Captopril-treated animals were indistinguishable from controls. A total of seven animals were sacrificed in extremis from tumour growth or lung damage prior to their scheduled autopsy time, and two animals died prematurely of other causes. Of these nine cases, only two were Captopril-treated animals.

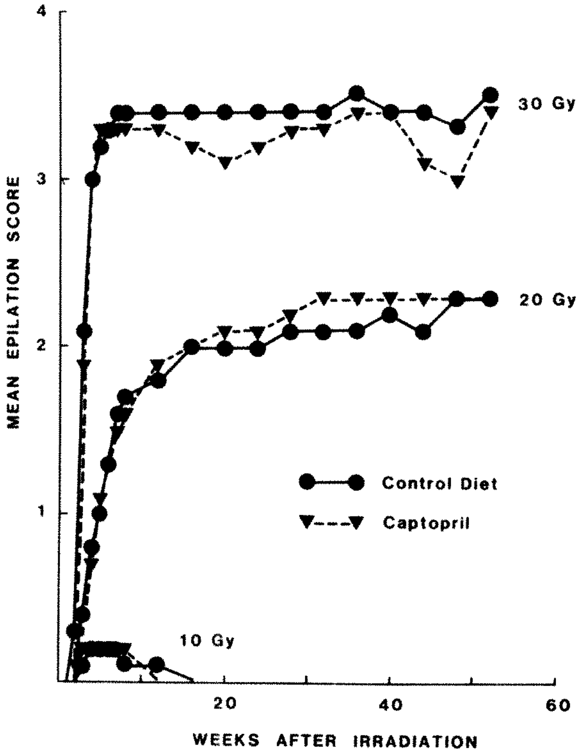

Figure 1. Mean epilation score as a function of time (weeks) after irradiation in rats consuming either control diet (circles) or feed containing 0.08% (w/w) Captopril (triangles) continuously after irradiation. See text for scoring criteria. The SEM for all data points was ±0.1, and was omitted for graphic clarity. Analysis of variance revealed that Captopril had no significant effect on epilation.

Epilation

Hair loss in the radiation port was minor and transient (3–12 weeks) after 10 Gy, but became increasingly severe and permanent with increasing radiation dose (Fig. 1). In animals exposed to 30 Gy, epilation appeared at 2 weeks post-irradiation, reached a peak at 7 weeks, then persisted essentially unchanged through 52 weeks. The severity of epilation in animals receiving Captopril was not significantly different from that in control animals at any radiation dose (Fig. 1).

Moist desquamation

Moist desquamation was not observed after 0 or 10 Gy, and was rare after 20 Gy in both the control and Captopril-treated animals (Table I). In rats exposed to 30 Gy, however, two waves of moist desquamation were

Table I. Effect of Captopril on moist desquamation in irradiated rat skin

Week	20 Gy		30 Gy	
	Control	Captopril	Control	Captopril
1	0.0 ± 0.0[a]	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
2	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.1	0.1 ± 0.1
3	0.1 ± 0.1	0.1 ± 0.1	1.4 ± 0.2	1.5 ± 0.2
4	0.2 ± 0.1	0.1 ± 0.1	2.8 ± 0.2	2.8 ± 0.2
5	0.3 ± 0.1	0.2 ± 0.1	3.1 ± 0.2	3.0 ± 0.2
6	0.1 ± 0.1	0.1 ± 0.1	3.2 ± 0.2	2.9 ± 0.2
7	0.2 ± 0.1	0.2 ± 0.1	3.3 ± 0.2	3.0 ± 0.1
8	0.2 ± 0.1	0.3 ± 0.1	3.2 ± 0.2	2.9 ± 0.2
10	0.2 ± 0.1	0.4 ± 0.1	3.2 ± 0.2	2.9 ± 0.2
12	0.2 ± 0.1	0.3 ± 0.1	3.0 ± 0.2	2.7 ± 0.2
14	0.2 ± 0.1	0.5 ± 0.1	2.9 ± 0.2	2.3 ± 0.2[b]
16	0.3 ± 0.1	0.4 ± 0.1	2.9 ± 0.2	2.5 ± 0.3[b]
18	0.4 ± 0.1	0.5 ± 0.1	2.9 ± 0.2	2.5 ± 0.3[b]
20	0.4 ± 0.1	0.5 ± 0.1	2.8 ± 0.2	2.4 ± 0.2[b]
22	0.3 ± 0.1	0.5 ± 0.2	2.8 ± 0.2	2.4 ± 0.3[b]
24	0.4 ± 0.2	0.6 ± 0.2	2.7 ± 0.3	2.5 ± 0.2
28	0.3 ± 0.2	0.7 ± 0.3	3.1 ± 0.3	2.9 ± 0.3
32	0.5 ± 0.2	0.5 ± 0.2	3.2 ± 0.3	2.7 ± 0.3[b]
36	0.8 ± 0.3	0.5 ± 0.2	3.1 ± 0.3	2.8 ± 0.3
40	0.7 ± 0.2	0.6 ± 0.3	2.8 ± 0.4	2.8 ± 0.3
44	0.7 ± 0.4	1.0 ± 0.3	2.1 ± 0.6	2.4 ± 0.5
48	0.9 ± 0.3	1.3 ± 0.3	2.0 ± 0.6	1.9 ± 0.6
52	1.4 ± 0.3	1.4 ± 0.3	2.0 ± 0.6	1.7 ± 0.5

[a] Mean ± SEM; n = 32 to week 14, 24 to week 26, 16 to week 40, and 8 to week 52. Moist desquamation was scored on a scale from 0 = none, 1.0 = surface intact but irregular, 2.0 = few small scattered foci, 3.0 = involving less than half of port and 4.0 = involving more than half of port. Animals exposed to 0 or 10 Gy and consuming either diet exhibited no moist desquamation throughout the study.

[b] Different from control, $p < 0.05$.

observed. The first wave occurred at 3 weeks post-irradiation, reached a peak at 6–10 weeks, then resolved partially but significantly from 12 to 26 weeks post-irradiation (Table I). The second wave of moist desquamation began at 26–28 weeks, reached a peak at 30–32 weeks, and then subsided irregularly through 52 weeks (Table I). The second wave of desquamation was often ulcerative and precipitous, occasionally exhibiting almost complete breakdown of a previously intact skin surface within a 1 week period. Multiple analysis of variance revealed that the mean desquamation score after 30 Gy was significantly ($p < 0.05$) lower in animals receiving Captopril than in the control animals (Table I). The biphasic nature of the moist desquamation reaction could be seen clearly when the incidence (%) of animals exhibiting the most severe reaction, 4.0 (involving more than half of the port) was plotted as a function of time after 30 Gy (Fig. 2). Captopril reduced the area under both waves by approximately one-third ($p < 0.05$). The ACE inhibitor did not influence the time of onset of either wave, rather it reduced the peak incidence and accelerated the resolution of both phases of the moist desquamation reaction (Fig. 2). As a result, Captopril-treated animals exhibited a third wave of severe desquamation at 38–40 weeks, which was masked in the control animals (Fig. 2).

Carcinogenesis

A total of 14 tumours was observed in the radiation ports of 11 rats during the study, and all were fibrosarcomas or squamous cell carcinomas (Table II). Most tumours were detected 36 weeks or longer after 30 Gy. Of the 14 tumours, only three ($\chi^2 = 4.57$, $p < 0.05$) were detected in rats receiving Captopril. Multiple tumours (three cases), tumours induced by 20 Gy (three cases), and tumours appearing before 26 weeks (one case) were observed only in rats consuming control diet, never in Captopril-treated animals (Table II). Rats developing tumours in the second 6 months post-irradiation exhibited significantly more severe moist desquamation during the first 6 months than did the tumour-free members of their treatment group (Table III).

Discussion

These data are the first to demonstrate that the ACE inhibitor Captopril reduces radiation reactions in skin. Thus skin represents the third organ, along with kidney (Robbins & Hopewell, 1986) and lung (Ward & Hinz, 1987; Ward et al, 1988), whose radiation response can be modified by this compound. The two waves of moist desquamation observed after 30 Gy are a well-documented response to high doses of radiation in several species (Field, 1969; Hopewell, 1986). It has been

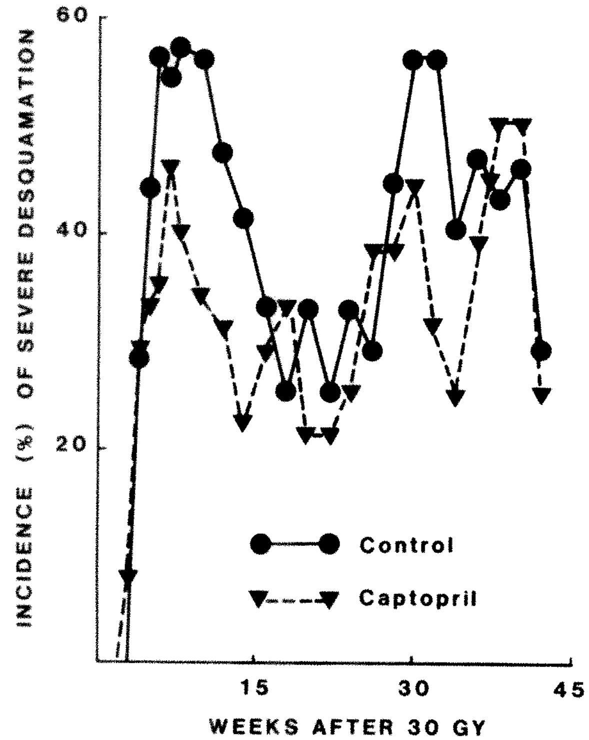

Figure 2. Incidence (%) of severe moist desquamation (score of 4.0 = involving more than half of the radiation port) as a function of time (weeks) after exposure to 30 Gy of ^{60}Co γ rays in rats consuming either control diet (circles) or feed containing 0.08% (w/w) Captopril (triangles) continuously after irradiation.

proposed that the first wave results from epithelial damage; and the second, from vasculo-connective tissue damage (Hopewell, 1986). The present study was not designed to test this possibility, but Captopril reduced both waves by approximately the same extent (*i.e.* by one-third).

The mechanism of Captopril's therapeutic action in this model is not clear at present. Captopril is not only an ACE inhibitor but also a thiol compound, and the presence of the sulphhydryl moiety appears to account for some (but only some) of the drug's radiation modifying activity in lung (Ward et al, 1989). We do not know whether a non-thiol ACE inhibitor would exhibit the same sparing effect on radiation skin reactions as does Captopril. Regardless of mechanism, Captopril can be added to the list of agents known to ameliorate skin damage when administered after irradiation. These agents include anti-inflammatory compounds (Bjornberg et al, 1965; Bielicky et al, 1966; Chung et al, 1972), L-triiodothyronine (Glicksman et al, 1959; Kitagawa et al, 1961) and pentoxifylline (Dion et al, 1989). Interestingly, anti-inflammatory agents reduce the severity of radiation-induced skin ulcers without influencing epilation (Chung et al, 1972), as does Captopril. Captopril is not commonly regarded as an anti-inflammatory agent, although it does exhibit that action in patients with rheumatoid arthritis (Martin et al, 1984).

These data also are the first to demonstrate that Captopril reduces the incidence of malignancies in the radiation treatment field. The mechanism of this anticarcinogenic action is unknown, although tumourigenesis and severe desquamation may not be entirely independent events. All animals which developed tumours during the second 6 months exhibited severe desquamation during the first wave of skin reaction at 6–10 weeks post-irradiation. Captopril perhaps reduced the pool of animals at risk by reducing the frequency of severe early desquamation, and thereby indirectly decreased the incidence of tumours. As a thiol, however, it is possible that Captopril exhibited a more direct anticarcinogenic action. Thiols such as cysteamine protect against carcinogenesis when given before radiation (Milas et al, 1984); however, we administered Captopril only after irradiation. The thiol WR-1065 reduces mutagenesis when given after irradiation (Grdina et al, 1985), although the longest post-radiation time interval tested in that study was 3 h. Captopril is now known to be a radical scavenger (Westlin & Mullane, 1988; Chopra et al, 1989) and to form copper complexes possessing antioxidant activity (Roberts & Robinson, 1985; Christie et al, 1988). These molecular mechanisms might reduce chronic events in radiation pathophysiology and carcinogenesis. As an inhibitor of

Table II. Tumours in the radiation port

Rat no.	Dose (Gy)	Diet	Histology	Foci	Week detected
2796	30	Captopril	Fibrosarcoma	Single	46
2799	30	Control	Fibrosarcomas	Multiple	52
2818	30	Captopril	Squamous cell ca	Single	37
2821	30	Control	Fibrosarcomas	Multiple	36, 37
2827	30	Captopril	Fibrosarcoma	Single	49
2838	30	Control	Fibrosarcoma	Single	52
2842	30	Control	Squamous cell ca	Single	52
2851	30	Control	Fibrosarcoma, squamous cell ca	Multiple	47
2854	20	Control	Squamous cell ca	Single	39
2881	20	Control	Squamous cell ca	Single	37
3071	20	Control	Squamous cell ca	Single	24

Table III. Moist desquamation in tumour-free and tumour-bearing rats

Week	20 Gy control		30 Gy control		30 Gy captopril	
	No tumour	tumour	No tumour	tumour	No tumour	tumour
4	0.2±0.1[a]	0.0±0.0	2.7±0.2	4.0±0.0	2.8±0.2	3.7±0.3
8	0.2±0.1	0.3±0.3	3.1±0.2	4.0±0.0	2.8±0.2	4.0±0.0
12	0.1±0.1	0.3±0.3	2.9±0.2	4.0±0.0	2.6±0.2	4.0±0.0
16	0.1±0.1	1.0±0.6	2.9±0.3	3.0±0.0	2.3±0.3	4.0±0.0
20	0.2±0.1	1.7±0.3	2.8±0.3	3.0±0.6	2.3±0.3	3.3±0.3
24	0.2±0.1	1.7±0.9	2.7±0.3	3.0±0.6	2.5±0.3	3.0±0.6

[a] Mean ± SEM. Moist desquamation was scored on a scale from 0 = none, 1.0 = surface intact but irregular, 2.0 = few small scattered foci, 3.0 = involving less than half of port and 4.0 = involving more than half of port. Tumours developed from 24–50 weeks after irradiation. No tumours occurred in Captopril-treated rats exposed to 20 Gy.

ACE (a peptidase), Captopril also may exhibit some of the properties of protease inhibitors. That property most relevant to the present discussion is the suppressive effect of protease inhibitors on radiation carcinogenesis *in vitro* (Kennedy & Little, 1978, 1981; Kennedy & Billings, 1987) and on chemical carcinogenesis *in vivo* (Weed et al, 1985; Messadi et al, 1986). Of particular interest is evidence that protease inhibitors are anticarcinogenic even when administered after irradiation (Kennedy, 1982).

In conclusion, the ACE inhibitor Captopril administered continuously after irradiation reduces benign and malignant skin reactions in rats. Furthermore, Captopril is effective at a regimen (25–50 mg/kg/day, p.o.) which appears to be free of significant side-effects for up to 1 year in this species. This regimen is approximately 12–25 times higher than the clinical antihypertensive regimen of 2 mg/kg/day (Gavras & Gavras, 1987). An agent which reduces both the severity of radiation-induced normal tissue injury and the risk of a second malignancy in the treatment field is to our knowledge unprecedented, and merits further study.

Acknowledgments

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References

Bielicky, T., Zak, M., Bartak, P. & Malina, L., 1966. Effect of chloroquine-diphosphate administration on the skin damage in guinea pigs caused by x-ray irradiation. *Journal of Investigative Dermatology*, *47*, 73–77.

Bjornberg, A., Hellgren, L. & Olsson, S., 1965. Treatment of radiation dermatitis with fluocinolone acetonide. *Acta Radiologica Therapy Physics Biology*, *3*, 129–134.

Chopra, M., Scott, N., McMurray, J., McLay, J., Bridges, A., Smith, W. E. & Belch, J. J. F., 1989. Captopril: a free radical scavenger. *British Journal of Clinical Pharmacology*, *27*, 396–399.

Christie, G. L., Hughes, M. A., Rees, S. B. & Williams, D. R., 1988. The binding of metal ions by Captopril (SQ14225). Part II. Complexation of copper (II). *Inorganica Chimica Acta*, *151*, 215–225.

Chung, J., Song, C. W., Yamaguchi, T. & Tabachnick, J., 1972. Effect of anti-inflammatory compounds on β-irradiation induced radiodermatitis. *Dermatologica*, *144*, 97–107.

Dion, M. W., Hussey, D. H. & Osborne, J. W., 1989. The effect of pentoxifylline on early and later radiation injury following fractionated irradiation in C3H mice. *International Journal of Radiation Oncology, Biology, Physics*, *17*, 101–107.

Field, S. B., 1969. Early and late reactions in skin of rats following irradiation with x-rays or fast neutrons. *Radiology*, *92*, 381–384.

Franciosa, J. A., 1987. The use of ACE inhibitors in congestive heart failure. In *Angiotensin Converting Enzyme Inhibitors*, ed. by J. B. Kostis and E. A. DeFelice (Liss, New York), pp. 123–148.

Gavras, I. & Gavras, H., 1987. The use of ACE inhibitors in hypertension. In *Angiotensin Converting Enzyme Inhibitors*, ed. by J. B. Kostis and E. A. DeFelice (Liss, New York), pp. 93–122.

Glicksman, A. S., Rawson, R. W. & Nickson, J. J., 1959. Modification of late radiation injury with L-triiodothyronine. *Radiology*, *73*, 178–190.

Grdina, D. J., Nagy, B., Hill, C. K., Wells, R. L. & Peraino, C., 1985. The radioprotector WR1065 reduces radiation-induced mutations at the hypoxanthina-guanine phosphoribosyl transferase locus in V79 cells. *Carcinogenesis*, *6*, 929–931.

Hopewell, J. W., 1986. Mechanisms of the action of radiation on skin and underlying tissues. In *Radiation Damage to Skin* (BJR Suppl. 19), ed., by H. Jammet et al (BIR, London), pp. 39–47.

Kennedy, A. R., 1982. Antipain, but not cycloheximide, suppresses radiation transformation when present for only one day at five days post-irradiation. *Carcinogenesis*, *3*, 1093–1095.

Kennedy, A. R. & Billings, P. C., 1987. Anticarcinogenic action of protease inhibitors. In *Anticarcinogenesis and Radiation Protection*, ed. by P. A. Cerutti, O. F. Nygaard and M. G. Simic (Plenum Press, New York), pp. 285–295.

Kennedy, A. R. & Little, J. B., 1978. Protease inhibitors suppress radiation induced malignant transformation in vitro. *Nature (London)*, *276*, 825–826.

Kennedy, A. R. & Little, J. B., 1981. Effects of protease inhibitors on radiation transformation in vitro. *Cancer Research*, *41*, 2103–2108.

KITAGAWA, T., GLICKSMAN, A. S., TYREE, E. B. & NICKSON, J. J., 1961. Radiation effects on skin and subcutaneous tissue. A quantitative study of collagen content: modification with L-triiodothyronine. *Radiation Research, 15*, 761–766.

MARTIN, M. F. R., MCKENNA, F., BIRD, H. A., SURRALL, E. K., DIXON, J. S. & WRIGHT, V., 1984. Captopril: a new treatment for rheumatoid arthritis? *Lancet, 1*, 1325–1328.

MESSADI, D. V., BILLINGS, P., SHKLAR, G. & KENNEDY, A. R., 1986. Inhibition of oral carcinogenesis by a protease inhibitor. *Journal of the National Cancer Institute, 76*, 447–452.

MILAS, L., HUNTER, N., STEPHENS, L. C. & PETERS, L. J., 1984. Inhibition of radiation carcinogenesis in mice by S-2-(3-aminopropyl amino)-ethylphosphorothioic acid. *Cancer Research, 44*, 5567–5569.

ROBBINS, M. E. C. & HOPEWELL, J. W., 1986. Physiological factors affecting renal radiation tolerance: a guide to the treatment of late effects. *British Journal of Cancer, 53 (Suppl. VII)*, 265–267.

ROBERTS, N. A. & ROBINSON, P. A., 1985. Copper chelates of antirheumatic and anti-inflammatory agents and their superoxide dismutase-like activity and stability. *British Journal of Rheumatology, 24*, 128–136.

WARD, W. F. & HINZ, J. M., 1987. Prostacyclin and thromboxane production by irradiated rat lung. In *Prostaglandin and Lipid Metabolism in Radiation Injury*, ed. by T. L. Walden, Jr. and H. N. Hughes (Plenum Press, New York), pp. 147–158.

WARD, W. F., KIM, Y. T., MOLTENI, A. & SOLLIDAY, N. H., 1988. Radiation-induced pulmonary endothelial dysfunction in rats: modification by an inhibitor of angiotensin converting enzyme. *International Journal of Radiation Oncology, Biology, Physics, 15*, 135–140.

WARD, W. F., MOLTENI, A., KIM, Y. T. & TS'AO, C., 1989. Structure–function analysis of angiotensin-converting enzyme inhibitors as modifiers of radiation-induced pulmonary endothelial dysfunction in rats. *British Journal of Radiology, 62*, 348–354.

WARD, W. F., MOLTENI, A., TS'AO, C. & SOLLIDAY, N. H., 1987. Pulmonary endothelial dysfunction induced by unilateral as compared to bilateral thoracic irradiation in rats. *Radiation Research, 111*, 101–106.

WEED, H., MCGANDY, R. B. & KENNEDY, A. R., 1985. Protection against dimethylhydrazine induced adenomatous tumors of the mouse colon by the dietary addition of an extract of soybeans containing the Bowman–Birk protease inhibitor. *Carcinogenesis, 6*, 1239–1241.

WESTLIN, W. & MULLANE, K., 1988. Does Captopril attenuate reperfusion-induced myocardial dysfunction by scavenging free radicals? *Circulation, 77 (Suppl. I)*, 130–139.

ZAR, J. R., 1974. *Biostatistical Analysis* (Prentice–Hall, Englewood Cliffs, NJ), pp. 121–181.

1990, *The British Journal of Radiology*, *63*, 355–356

Technical note

The variation of wedge factors with field size on a linear accelerator

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When a wedge filter is used to modify the dose distribution in a beam of megavoltage X-rays, the beam intensity is reduced. The reduction of beam intensity is quantified by a factor called the wedge factor (WF) defined as follows:

$$\mathrm{WF} = \frac{\text{absorbed dose per monitor unit with wedge}}{\text{absorbed dose per monitor unit without wedge}}$$

where measurements are performed in water at the depth of maximum build-up.

It is assumed by the authors of several treatment planning systems that the wedge factor doses do not vary with field size. Palta et al (1988) presented measurements for a range of square field sizes with 4 MV and 6 MV X rays, showing that there can be considerable variation of wedge factor with field size, especially for a 60° wedge, and that errors in dose of up to 7% can occur by ignoring this variation.

This technical note presents the results of similar measurements on 8 MV and 16 MV beams with a 60° wedge. The variation of wedge factor for a range of rectangular field sizes has also been investigated; this was done to see whether the variation follows an equivalent square law, or whether one should follow the practice of one commercial planning system by considering only the dimension in the wedged direction.

Methods and materials

A Dynaray LA20 linear accelerator (Asea-Brown-Boveri) was used to produce X rays at two energies. The lower energy is of nominal energy 8 MV, the higher energy 16 MV. It has a single wedge, the wedge angle of which is 58° at 8 MV and 60° at 16 MV. Fields with smaller wedge angles are produced using a mixture of wedged and unwedged fields in a method similar to that described by Tatcher (1970). The largest possible beam width at the isocentre for a wedged field is 20 cm. The largest possible length is 40 cm.

Measurements were performed at 100 cm source–skin distance in a water tank at the depth of maximum build-up (2.0 cm for 8 MV, 3.0 cm for 16 MV). A PTW 0.3 cm^3 ionization chamber was used, connected to a PTW SN4 electrometer. The axis of the chamber was perpendicular to the direction of wedging. Measurements were made of electrometer reading per 100 monitor units, with several readings being done alternately with and without wedge. The measurements were repeated with the wedge rotated through 180°, and an average ratio calculated.

Measurements of wedge factor were made for the following field sizes for 8 MV: 5 cm × 5 cm, 10 cm × 10 cm, 12.5 cm × 12.5 cm, 15 cm × 15 cm, 20 cm × 20 cm, 5 cm × 10 cm, 10 cm × 16.7 cm, 15 cm × 30 cm, 20 cm × 40 cm, 10 cm × 5 cm and 20 cm × 10 cm. The first quoted value in each case is the wedged dimension. The following sizes were used at 16 MV: 5 cm × 5 cm, 10 cm × 10 cm, 15 cm × 15 cm, 20 cm × 20 cm, 5 cm × 10 cm, 10 cm × 20 cm, 15 cm × 30 cm, 20 cm × 40 cm, 10 cm × 5 cm and 20 cm × 10 cm.

Results

The variation of wedge factor with field size is shown in Figs 1 and 2, for 8 MV and 16 MV, respectively. The square symbols are for square fields. The data for rectangular fields have been plotted twice: the crosses show the values plotted against the dimension in the wedged direction, the diamonds show the same values plotted against the equivalent square field calculated using the well established formula $2xy/(x+y)$ (Worthley, 1966).

For both energies, the latter points lie within 1% of a curve drawn through the values for square fields, whilst the values plotted by wedged dimension differ from the

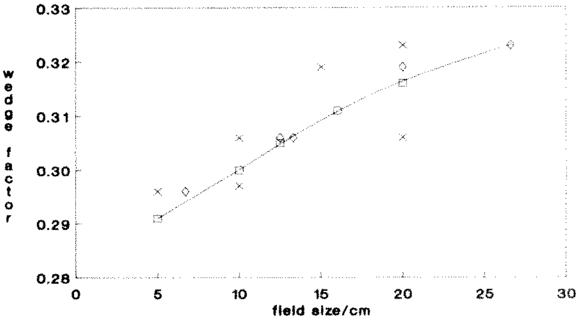

Figure 1. Wedge factor for 8 MV X rays against field size in cm. The square points are for square fields, the diamonds for rectangular fields plotted by equivalent square size, the crosses for rectangular fields plotted by dimension in the wedged direction.

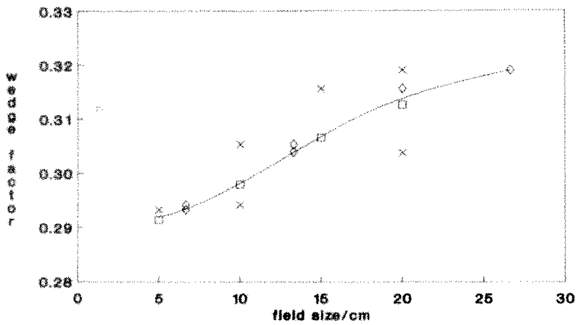

Figure 2. Wedge factor for 16 MV X rays against field size in cm. The square points are for square fields, the diamonds for rectangular fields plotted by equivalent square size, the crosses for rectangular fields plotted by dimension in the wedged direction.

curves by as much as 3%. If a single wedge factor (*e.g.* that measured for a 10 cm × 10 cm field) was used at each energy, errors in doses of up to 7% could occur at 16 MV, or over 8% at 8 MV; these values are similar to the 7% reported by Palta et al (1988) using a 60° wedge on a Philips SL75/5.

Discussion

Several treatment planning systems do not allow for variation of wedge factor with field size, and require the use of a single factor for each wedge at a given energy. This can lead to considerable errors. One commercially available treatment planning system allows values for several square field sizes to be entered, but does not interpolate between entered values; instead it uses each entered value over a range of field size, selected solely by the size in the wedged direction. Whilst this is better than nothing, it can still lead to errors of several per cent, especially for elongated fields.

It would appear from these results that the best approach for a treatment planning program would be to use values for three or four field sizes, including the largest and smallest sizes in clinical use, and to interpolate between these values on the basis of the equivalent square field sizes.

References

WORTHLY, B., 1966. Equivalent squares of rectangular fields. *British Journal of Radiology, 39,* 559.

TATCHER, M., 1970. A method for varying effective angle of wedge filters. *Radiology, 97,* 132.

PALTA, J. R., DAFTARI, I. & SUNTHARALINGAM, N., 1988. Field size dependence of wedge factors. *Medical Physics, 15,* 624–626.

1990, *The British Journal of Radiology*, *63*, 357–360

Case reports

Calcification of the large bowel in schistosomiasis demonstrated by computed tomography

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Calcification within the urinary tract and seminal vesicles is a common sequel of *Schistosoma haematobium* infection (Delahaye, 1977; Cockshott & Middlemiss, 1979). Local granulomatous reaction and fibrosis follow the deposition of ova in the walls of these organs. The calcification occurs within dead ova. A similar chronic inflammatory response follows the deposition of the ova of *Schistosoma mansoni* in radicles of the mesenteric venous system. Unlike the genitourinary tract, intestinal calcification has rarely been recorded in schistosomal infection (Lehman et al, 1971; Fataar et al, 1985).

Four patients from an area where *S. mansoni* is endemic are described, each of whom showed intestinal calcification on computed tomography.

Case reports

Case 1

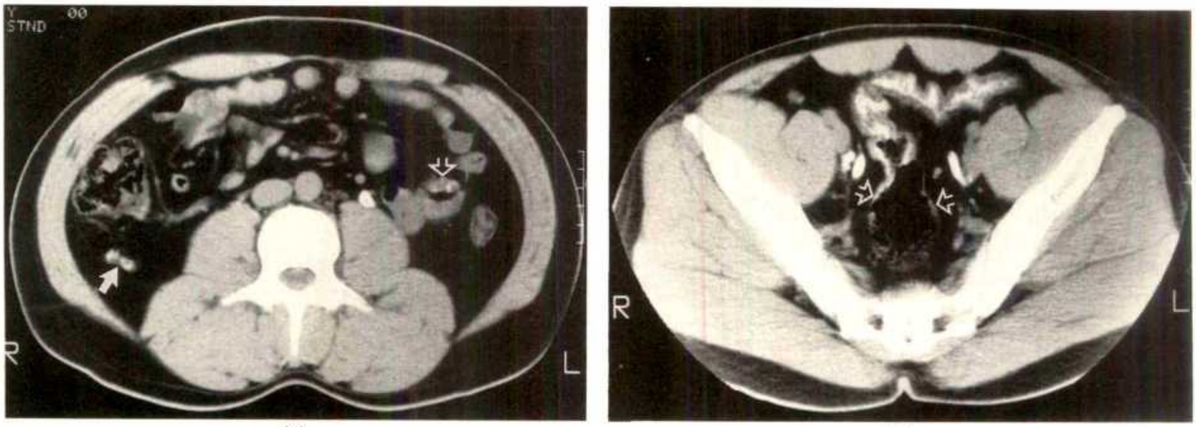
A 23-year-old Egyptian male with a past history of urinary schistosomiasis complained of infertility, dysuria and haematuria. A plain radiograph of the abdomen demonstrated calcification of the urinary bladder and both ureters throughout their length, as well as densely calcified seminal vesicles. Faint linear calcification was also apparent in the ascending and descending segments of the colon and in the appendix. A computed tomographic (CT) scan confirmed the calcifications seen in the genitourinary tract and large bowel. In addition, extensive calcification was apparent in the rectum and sigmoid colon (Fig. 1).

Case 2

A 49-year-old Egyptian male presented with left loin pain and dysuria. There were no gastrointestinal symptoms. A plain radiograph of the abdomen revealed calcification of the urinary bladder, left ureter and the seminal vesicles. Linear calcification was noted in the right iliac fossa. A CT scan showed extensive mural calcification within all segments of the large bowel from the rectum to the caecum (Fig. 2). In addition, there was calcification in the left lateroconal fascia.

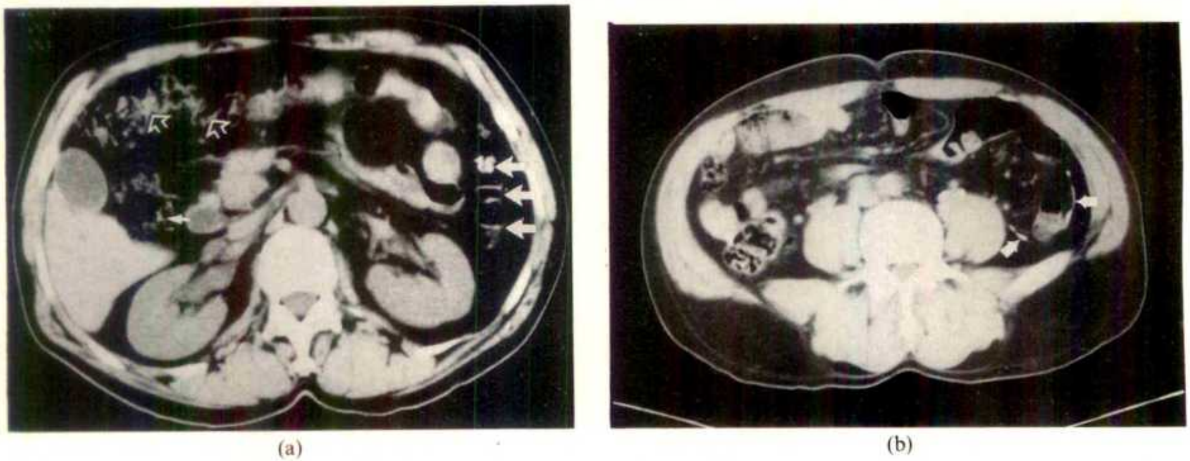
Case 3

A 30-year-old Egyptian male complained only of right renal colic. Plain radiography revealed calcification in the urinary bladder, seminal vesicles and rectum, well shown on CT (Fig. 3).



(a) (b)

Figure 1. *Case 1*. (a) Calcification seen in the appendix (closed arrow), the wall of the caecum and the descending colon (open arrow). The left ureter is also heavily calcified. (b) Extensive calcification in sigmoid colon and also in rectum (arrows). Note the heavy ureteric calcification.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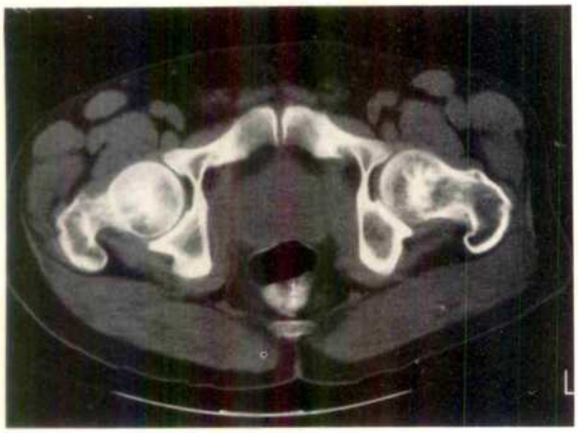
(c)

Figure 2. *Case 2.* Mural calcification within (a) ascending (small solid arrow), transverse (open arrows) and descending colon (large solid arrows), (b) ascending and descending colon and left lateroconal fascia (arrows) and (c) within a mass in the posterior aspect of rectum (pixel attenuation value 262 Hounsfield units) and in a curvilinear distribution within the anterior wall of rectum.

Case 4

A 39-year-old Yemeni complained of recurrent bouts of haematemesis, melena and subacute intestinal obstruction. On examination he was severely anaemic with signs consistent with hepatic cirrhosis and portal hypertension. A CT scan of the abdomen showed heavy mural calcification in the sigmoid colon and in the rectum (Fig. 4). There was marked perirectal soft-tissue thickening, consistent with fibrosis.

Discussion

Intestinal schistosomiasis results from infection by the trematode parasite *Schistosoma mansoni*. There is a high incidence of *S. mansoni* in the Nile Valley and a focal distribution in the Middle East, including the Yemen and parts of Saudi Arabia. It also occurs widely throughout Africa as well as in South America and the Caribbean.

The adult worms of *S. mansoni* migrate from the portal vein to mesenteric venous radicles in the intestinal wall, where the main egg laying takes place. Inflammatory reaction around the eggs causes irregular mucosal thickening, the formation of granulomatous

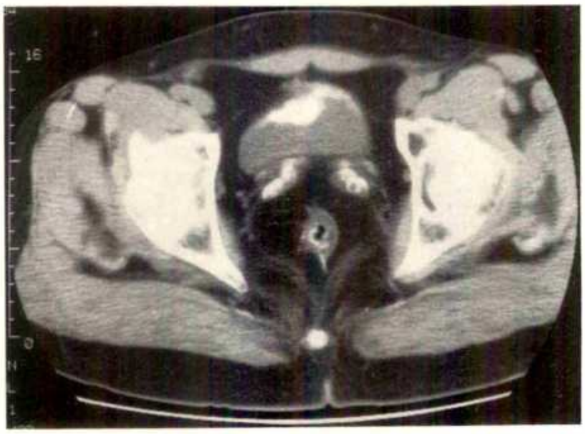

Figure 3. *Case 3.* Calcification is visible within the rectal submucosa, seminal vesicles and urinary bladder.

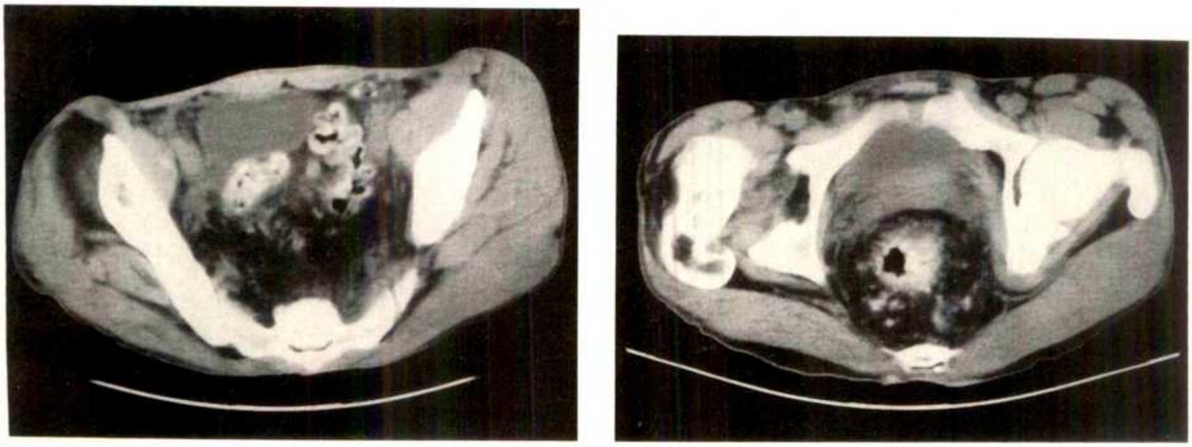
(a) (b)

Figure 4. *Case 4.* (a) Heavy calcification of sigmoid colon and (b) marked perirectal thickening with associated calcification.

polyps and eventually fibrosis of the intestinal wall. These changes are demonstrable on barium enema examination (Chait, 1963; Medina et al, 1965). Although changes occur most frequently in the distal part of the colon and the rectum, the proximal colon and small intestine may also be involved.

The migration of parasites to the hepatic radicles of the portal vein results in periportal fibrosis and, subsequently, portal hypertension with ascites and splenomegaly. Eggs from *S. mansoni* may be widely disseminated throughout the body. Characteristic granulomas sometimes form in the lungs, resulting in cor pulmonale.

The patient with intestinal schistosomiasis experiences colic and diarrhoea with the passage of blood and mucus, between 2 months and 2 years of the initial infection. Exacerbations of these symptoms tend to recur at 2 or 3 week intervals in the early stages of schistosomiasis. The engorged and hypertrophic intestinal mucosa becomes ulcerated and polypoid granulomas develop in the rectum and colon. The colon eventually becomes a fibrous tube, largely devoid of mucosa. At this stage, the patient may still complain of intermittent diarrhoea with mucus and blood as well as periods of remission (Maegraith, 1980).

Lehman et al (1971) were the first to describe intestinal calcification in a case of *S. mansoni.* Extensive amorphous calcification, seen within the left side of the abdomen on plain radiography was found to have a laminar distribution adjacent and parallel to the contrast column in a subsequent barium enema. Similar findings were also encountered by Fataar et al (1984) in 14 cases. As well as the linear calcification in the colonic wall, these authors also described calcification within the hypertrophic rectal mucosa converging towards the anal canal. In mixed *S. mansoni* and *S. haematobium* infection, rectal and urinary bladder calcification is seen. Fataar et al (1985) have described a case in which calcification in the sigmoid segment and rectum were demonstrated on CT, the rectal calcification being invisible on plain radiography. Radhakrishnan et al (1988) reported a case with calcification demonstrated in the liver and small intestine on CT.

Calcification is seen in more cases of *S. haematobium* than *S. mansoni* not only because more ova are laid in the former but also the ova calcify more readily (Cheever et al, 1977).

An interesting feature in Case 2 was the calcification in the left lateroconal fascia. As with the colonic calcification, the high CT number (317–365 Hounsfield units) of pixels confirms that the high density is calcification and not a windowing artefact. This extracolonic calcification demonstrates the wide dissemination of ova which may occur in *S. mansoni* infection.

The mural calcification of intestinal schistosomiasis is more likely to be demonstrated on CT, with its high inherent contrast, than on plain radiography. The increasing availability of computed tomography in areas where *S. mansoni* is endemic is likely to result in more frequent recognition of bowel calcification. As these cases demonstrate, there may be no recent symptoms of intestinal disease.

Summary

Four cases are described in which large bowel calcification was demonstrated on CT. All four patients had mixed infection by *Schistosoma haematobium* and *mansoni,* the latter being responsible for this abnormality. Intestinal calcification by *S. mansoni* is unusual, but is especially well demonstrated by computed tomography.

References

Cheever, A. W., Kamel, I. A., Elwi, A. M. Mosimann, J. E. & Danner, R., 1977. Schistosoma mansoni and S. haematobium infections in Egypt. II Quantitative parasitological findings at necropsy. *Americal Journal of Tropical Medicine and Hygiene*, *26*, 702–716.

Chait, A., 1963. Schistosomiasis mansoni: roentgenologic observations in a nonendemic area. *American Journal of Roentgenology*, *90*, 688–707.

Cockshott, P. & Middlemiss, H., 1979. *Clinical Radiology in the Tropics* (Churchill Livingstone, Edinburgh and London), pp. 110–112.

Delahaye, R.-P., 1977. *Radiologie Tropicale et Parasitaire.* (Delachaux et Niestle S.A., Neuchatel and Paris), pp. 133–134.

Fataar, S., Bassiony, H., Satyanath, S. et al, 1985. CT of schistosomal calcification of the intestine. *American Journal of Roentgenology*, *114*, 75–76.

Lehman, J. S., Farid, Z., Bassily, S. & Kent, D. C., 1971. Colonic calcification and polyposis in schistosomiasis. *Radiology*, *98*, 379–380.

Maegraith, B., 1980. *Clinical Tropical Diseases*, *7th edn* (Blackwell Scientific Publications, Oxford and London), pp. 383–389.

Medina, J. T., Seaman, W. B., Guzman-Acosta, C. & Diaz-Bonnet, R. B., 1965. The roentgen appearances of schistosomiasis mansoni involving the colon. *Radiology*, *85*, 682–688.

Radhakrishnan, S., Al Nakib, B., Sivanandan, R. & Menon, N. K., 1988. Hepatosplenic and small bowel calcification due to Schistosoma mansoni infection. *Digestive Diseases and Sciences*, *33*, 1637–1640.

Malignant struma ovarii: presentation and management

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Struma ovarii are rare tumours and just over 400 cases are reported in the world literature (Gould et al, 1983). The incidence of malignancy is reported as 5–10% of all cases of struma ovarii (Marcus & Marcus, 1961) but has been reported as less (Gould et al, 1983). The metastasis rate is estimated to be 5–6% (Emge, 1940) and only 21 cases with metastases have so far been reported (Dalley, 1970; Pardo-Mindan & Vazquez, 1983; Willemse et al, 1987; Rosenblum et al, 1989). Owing to their rarity, there is no universal agreement as to management. Surgical excision continues to remain the initial definitive primary treatment. However, metastatic and recurrent malignant struma ovarii have been treated with radioactive ^{131}I (Woodruff et al, 1966; Kempers et al, 1970; Willemse et al, 1987). Intra-peritoneal radiocolloids (Woodruff et al, 1966; Rosenblum et al, 1989) and external beam radiotherapy (Gonzalez-Angulo et al, 1963; Woodruff et al, 1966; Pardo-Mindan & Vazquez, 1983) have also found a useful role in palliation.

This paper describes the presentation and management of two patients with malignant struma ovarii referred to the Royal Marsden Hospital between 1945 and 1989, during which time nearly 3000 other ovarian tumours were recorded.

Case reports

Case 1

A 35-year-old married woman with no previous or family history of thyroid disease presented in 1951 with severe recurrent abdominal pain. Laparotomy was performed and both ovaries were found to be cystic. The right ovary was partly resected together with ligation of the right fallopian tube and left salpingo-oophorectomy was performed. Histology revealed a left ovarian teratoma containing thyroid tissue with areas of papillary thyroid carcinoma.

Three years later, she developed further pain and swelling on the right side of the pelvis. Laparotomy was performed and a ruptured thin-walled right ovarian cyst was removed. Unfortunately, histology was not available. In October, 1962, abdominal pain recurred and right salpingo-oophorectomy and hysterectomy together with omentectomy were performed. The right ovary measured 90 × 55 × 50 mm and weighed 225 g. The stump of the left ovary and the entire peritoneal cavity were studded with numerous tumour deposits up to 25 mm in diameter. There were also two small seedlings in the abdominal wall at the site of a previous operation scar. Histology of the ovarian tumour and the deposits revealed well differentiated adenocarcinoma of thyroid tissue with both follicular and papillary elements (Fig. 1).

In December 1962 she was referred to the Royal Marsden Hospital for further management. Radioiodine studies with ^{131}I demonstrated normal 24 h uptake in the neck and scanning (Fig. 2) showed the thyroid to be of normal size and position. There was no evidence of abdominal uptake (Fig. 3). She subsequently received 1850 MBq (50 mCi) ^{131}I orally in order to ablate the normal thyroid and permit uptake into known abdomino-pelvic metastases. She subsequently became

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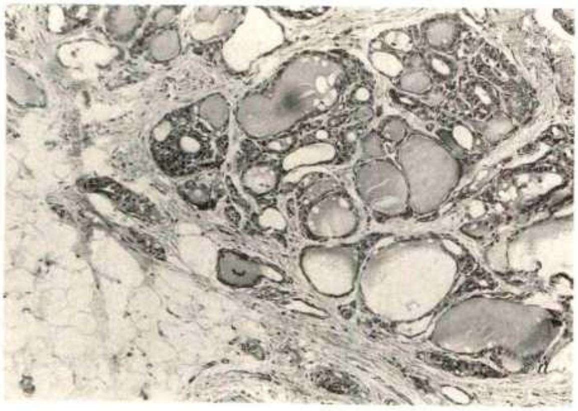

Figure 1. *Case 1.* Histology of omental metastases showing well differentiated adenocarcinoma of thyroid tissue with both follicular and papillary elements. (Haematoxylin × 160.)

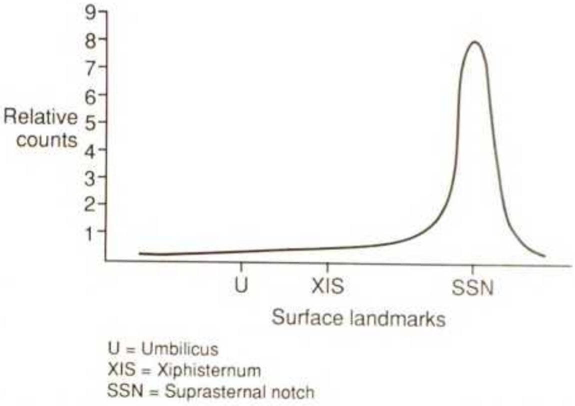

Figure 3. Whole-body profile scan showing uptake in neck only 24 h post-oral ^{131}I 3.7 MBq (100 μCi).

hypothyroid and has remained on L-Thyroxine 200 μg daily. She remains disease free 27 years later.

Case 2

A fit 35-year-old Maltese woman presented to her local hospital with a 6-month history of abdominal distension and back pain. Examination revealed a large mass arising from the pelvis extending up to the umbilicus. At laparotomy a macroscopically intact 15 cm diameter left ovarian mass was evident. The liver, mesentery and greater omentum appeared normal, as did the right ovary and uterus; there was no free fluid. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. Histology revealed that the left ovarian tumour consisted entirely of thyroid tissue with colloid follicles. Mitotic figures were present and in several areas the follicle lining cells showed nuclear pleomorphism and a high nuclear-cytoplasmic ratio. Review confirmed a well differentiated follicular adenocarcinoma with capsular invasion (Fig. 4).

She was subsequently referred to the Royal Marsden Hospital for further management. Clinically she was euthyroid with no abnormality in the neck. Abdominal examination revealed no abnormality other than a well healed laparotomy scar. Investigations including computed tomography (CT) and ultrasound showed no evidence of residual abdomino-pelvic disease. Bipedal lymphangiography showed reactive nodes only on the left side of the pelvis. Thyroid ultrasound and pertechnetate scanning showed no abnormality. Thyroid function tests and other haematological and biochemical tests were normal. Serum thyroglobulin was within normal limits (10 μg/l).

Staging investigations confirmed a Stage Ia malignant struma ovarii of the left ovary (International Federation of Gynecology and Obstetrics). Following her initial

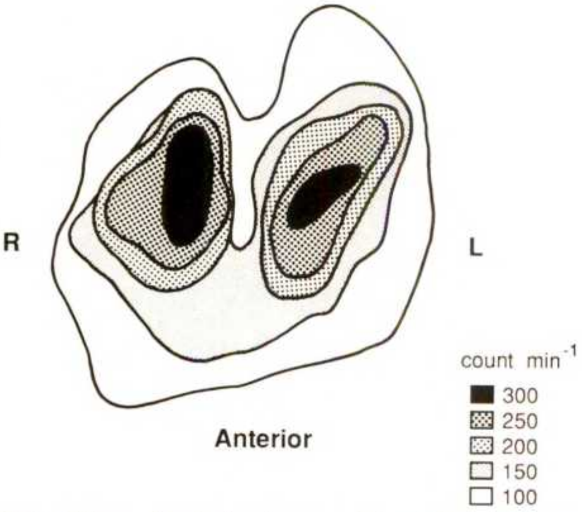

Figure 2. Scan of neck showing normal thyroid 24 h post-oral ^{131}I 3.7 MBq (100 μCi).

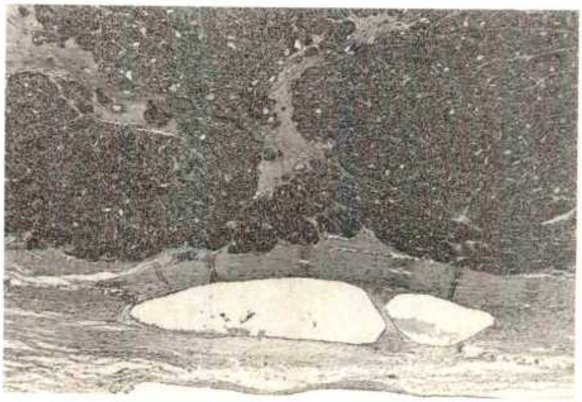

Figure 4. *Case 2.* Histology showing edge of left ovarian tumour with thyroid follicles eroding into the capsule. (Haematoxylin × 64.)

definitive surgery, management has consisted of a careful "watch policy" using serum thyroglobulin as a tumour marker at 3-month intervals together with abdomino-pelvic imaging (CT or ultrasound). Laparoscopy has been performed at 6-month intervals with peritoneal fluid cytology and thyroglobulin assay. Currently she remains in complete remission. Interestingly, her father died of bone metastases from a poorly differentiated follicular thyroid carcinoma.

Discussion

Thyroid tissue within an ovarian dermoid was first described by Böttlin in 1889 and its origin from dermoids or teratomas postulated by Pick in 1901. The term "struma ovarii colloides" was used by Meyer in 1903 and it is now accepted that these tumours are composed of true thyroid tissue arising in an ovarian teratoma (Marcus & Marcus, 1961).

Histological criteria of thyroid malignancy must include some features of cellular atypia, increased cellularity, nuclear pleomorphism and mitotic activity (Kempers et al, 1970). However, some authors argue that the only reliable criteria are capsule or blood vessel invasion, or dissemination (Tagerman, 1982). Similarities exist between malignant struma ovarii and cervical thyroid gland carcinoma (Yannopoulos et al, 1976; Willemse et al, 1987). In the absence of capsular invasion, prognosis is considered to be good. However, most malignant struma ovarii are follicular carcinomas whereas the papillary pattern is more commonly seen in cervical thyroid carcinoma.

The metastasis rate is low, estimated to be 5–6% (Emge, 1940) and may occur up to 26 years later (Kempers et al, 1970). Metastases are mostly abdominal implants with peritoneal spread to omentum and mesentery although blood borne metastases may occur in liver, brain, bone, lung, and contra-lateral ovary (Gonzalez-Angulo et al, 1963; Pardo-Mindan & Vazquez, 1983). Functioning metastatic sites have been demonstrated by scanning following the oral administration of radioiodine. Subtotal thyroidectomy followed by complete thyroid ablation with radioiodine has been advocated by some authors in order to enhance uptake in metastatic struma ovarii (Kempers et al, 1970; Willemse et al, 1987). Little or no uptake is to be expected with solid Hürthle-cell and anaplastic carcinomas.

In the first case described here, partial resection only was initially performed. Histology showed mixed papillary and follicular adenocarcinoma. When abdominal disease recurred 3 years later, ovarian cystectomy only was performed in spite of capsular rupture. At the time of definitive surgery, 11 years after the initial presentation, metastatic spread had occurred throughout the abdomen and pelvis. It is most likely that this patient's disease has been controlled by suppression of thyroid stimulating hormone rather than by radioiodine alone since no abdominal uptake was demonstrated.

Elevated serum thyroglobulin has proved to be of value as a marker of relapse for well differentiated thyroid carcinomas (Black et al, 1981). Thyroglobulin production has also been demonstrated in both benign and malignant struma ovarii (Hasleton et al, 1978) and raised serum thyroglobulin may be a useful marker of recurrent disease.

Most, if not all, tumours are diagnosed post-operatively and surgical excision remains the definitive primary treatment. Owing to the rarity of the tumour, however, there is no universal agreement as to the extent of surgery required, ranging from radical extirpation with total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and lymphadenectomy to a conservative approach with preservation of reproductive function. Since metastatic potential is low, unilateral salpingo-oophorectomy may be desirable in a young woman who has not yet completed her family provided there is no evidence of capsular invasion or dissemination at the time of surgery (Gould et al, 1983). More advanced disease should be treated by radical surgical excision with total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy. If residual abdominal disease is documented, subtotal thyroidectomy and radioactive ^{131}I therapy should be considered (Willemse et al, 1987). Thyroid hormone replacement is required thereafter. Similarly, recurrent and metastatic malignant struma ovarii have been treated with radioiodine (Woodruff et al, 1966; Kempers et al, 1970). Finally, external beam radiotherapy may offer useful palliation for metastases other than for widespread intra-abdominal disease and for those well differentiated and anaplastic carcinomas which do not concentrate radioiodine (Gonzalez-Angulo et al, 1963; Woodruff et al, 1966; Pardo-Mindan & Vazquez, 1983).

Acknowledgments

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References

BLACK, E. G., GIMLETTE, T. M. D., MAISEY, M. N., CASSONI, A., HARMER, C. L., OATES, G. D. & HOFFENBERG, R., 1981. Serum thyroglobulin in thyroid cancer. *Lancet, ii*, 443–445.

BÖTTLIN, R., 1889. Ueber Zahnentwickelung in Dermoidcysten des Ovariums. *Virchows Archiv für Pathologische Anatomie und Physiologie und für Klinische Medizin, 115*, 493–504.

DALLEY, V. M., 1970. Struma ovarii. In *Tumours of the Thyroid Gland*, ed. by Sir David Smithers (E. & S. Livingstone, Edinburgh), pp. 162–165.

EMGE, L. A., 1940. Functional and growth characteristics of struma ovarii. *American Journal of Obstetrics and Gynecology, 40*, 738–749.

GONZALEZ-ANGULO, A., KAUFMAN, R. H., BRAUNGARDT, C. D., CHAPMAN, F. C. & HINSHAW, A. J., 1963. Adenocarcinoma of thyroid arising in struma ovarii (Malignant struma ovarii). Report of two cases and review of the literature. *Obstetrics and Gynecology, 21*, 567–576.

GOULD, S. F., LOPEZ, R. L. & SPEERS, W. C., 1983. Malignant struma ovarii: a case report and literature review. *Journal of Reproductive Medicine, 28*, 415–419.

HASLETON, P. S., KELEHAN, P., WHITTAKER, J. S., BURSLEM, R. W. & TURNER, L., 1978. Benign and malignant struma ovarii. *Archives of Pathology and Laboratory Medicine*, *102*, 180–184.

KEMPERS, R. D., DOCKERTY, M. B., HOFFMAN, D. L. & BARTHOLOMEW, L. G., 1970. Struma ovarii—ascitic, hyperthyroid and asymptomatic syndromes. *Annals of Internal Medicine*, *72*, 883–893.

MARCUS, C. C. & MARCUS, S. L., 1961. Struma ovarii: a report of 7 cases and a review of the subject. *American Journal of Obstetrics and Gynecology*, *81*, 752–762.

MEYER, R., 1903. Struma ovarii colloides. *Virchows Archiv für Pathologische Anatomie und Physiologie und für Klinische Medizin*, *173*, 538–552.

PARDO-MINDAN, F. J. & VAZQUEZ, J. J., 1983. Malignant struma ovarii: light and electron microscopic study. *Cancer*, *51*, 337–343.

PICK, L., 1901. Die Marchandschen Nebennieren und ihre Neoplasmen: Nebst Utersuchungen über glykogenreiche Eierstocksgeschwulste. *Archiv für Gynäkologie*, *64*, 670–838.

ROSENBLUM, N. G., LIVOLSI, V. A., EDMONDS, P. R. & MIKUTA, J. J., 1989. Malignant struma ovarii. *Gynecologic Oncology*, *32*, 224–227.

TAGERMAN, A., 1982. Germ cell tumours of the ovary. In *Pathology of the Female Genital Tract*, ed. by A. Blaustein (Springer-Verlag, New York), pp. 636–639.

UICC, 1987. *TNM Classification of Malignant Tumours, 4th edn* (International Union Against Cancer, Springer-Verlag, London).

WILLEMSE, P. H. B., OOSTERHUIS, J. W., AALDERS, J. G., PIERS, D. A., SLEIJFER, D. TH., VERMEY, A. & DOORENBOS, H., 1987. Malignant struma ovarii treated by ovariectomy, thyroidectomy and 131-I administration. *Cancer*, *60*, 178–182.

WOODRUFF, J. D., RAUH, J. T. & MARKLEY, R. L., 1966. Ovarian struma. *Obstetrics and Gynecology*, *27*, 194–201.

YANNOPOULOS, D., YANNOPOULOS, K. & OSSOWSKI, R., 1976. Malignant struma ovarii. *Pathology Annual*, *11*, 403–413.

Tuberculosis of the patella

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Tuberculosis causing an osteolytic lesion in the patella is very rare, having been reported on only four previous occasions. We present such a case and discuss the radiological features which help in differentiating tuberculosis from other similar lesions.

Case report

A 25-year-old man in good health presented with a 3 month history of pain, swelling and restriction of movement of the right knee. There were no systemic symptoms or other joint involvement. Examination of the knee revealed an effusion with minimal terminal restriction of flexion. Radiographs of the knee joint demonstrated swelling (Fig. 1) and an osteolytic lesion in the patella (Fig. 2). Radionuclide bone scans showed an area of increased uptake in the right patella; no other lesions were seen on the scan. A chest radiograph revealed no abnormality.

A patellectomy was performed; there was a small area of erosion on the patellar articular surface. Histopathology showed features of tuberculous osteomyelitis, and accordingly the patient was started on anti-tuberculous therapy.

Discussion

Although the knee joint is frequently affected by tuberculosis, isolated involvement of the patella is rare (Hartofilakidis-Garofalidis, 1969; Gimenez et al, 1987). To our knowledge, this is only the fifth such case in the English literature.

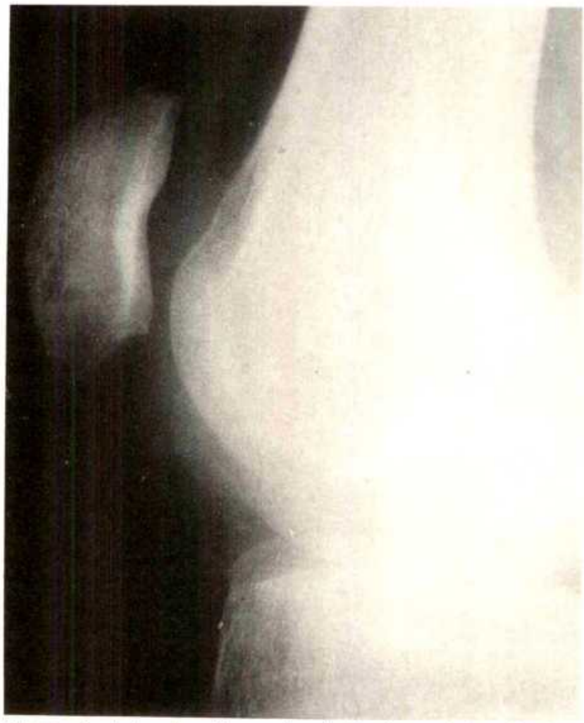

Figure 1. Lateral radiograph of the knee joint showing moderate osteoporosis and effusion. No effect on the articular surfaces is evident.

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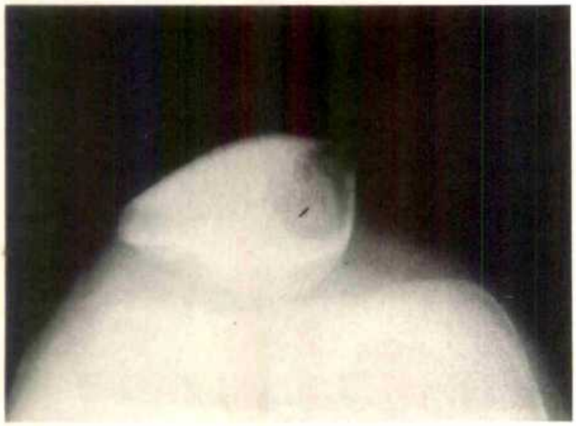

Figure 2. Axial view of the patella showing well-defined osteolytic lesion. Note that there is no sclerosis or sequestrum. No articular involvement is seen.

Osseous tuberculosis is usually believed to be due to hematogenous spread following a primary lesion in the lung. Tuberculous osteomyelitis is frequently associated with arthritis.

Cystic lesions in the patella are rare. The differential diagnosis of such a lesion includes cartilage-based tumours such as chondroblastoma and inflammatory lesions such as gout, pyogenic osteomyelitis or occasionally a brown tumour. The presence of a sequestrum and joint involvement suggest osteomyelitis. Absence of sclerosis around the lesion and in the para-articular region should suggest tuberculosis. When a tuberculous lesion is suspected, a radionuclide bone scan should be done as cystic tuberculosis of bone can affect several sites (O'Connor et al, 1970).

If a diagnosis is suspected radiologically, confirmation can be obtained by examination of the synovial fluid or by a synovial biopsy. The patient can then be treated with anti-tuberculous drugs without having to resort to a patellectomy.

References

GIMENEZ, M. H., BELTRAN, J. V. T., SEGUI, M. I. F. & GOMEZ, E. P., 1987. Tuberculosis of the patella. *Pediatric Radiology*, *17*, 328–329.

HARTOFILAKIDIS-GAROFALIDIS, G., 1969. Cystic tuberculosis of the patella. *The Journal of Bone and Joint Surgery*, *51A*, 582–585.

O'CONNOR, B. T., STEEL, W. M. & SANDERS, R., 1970. Dissiminated bone tuberculosis. *Journal of Bone and Joint Surgery*, *52A*, 537–540.

Raynaud's disease in childhood with radiological features

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(*Received September 1989*)

There have been many descriptions of Raynaud's phenomenon in adults (Allen & Brown, 1932; Gifford & Hines, 1957), but Raynaud's phenomenon has been only rarely reported in childhood, and Raynaud's disease itself is even more rare (Guntheroth et al, 1967; Burns et al, 1985). We describe here a 5-year-old boy with Raynaud's disease who had a 4-month history of pain, coldness and pallor of fingers in both hands on exposure to coldness. His right trans-femoral axillary arteriogram showed distal vascular abnormalities which were considerable owing to the peripheral arterial spasm. He had neither clinical haematological and serological evidence of collagen disease nor any other systemic disease, and has been successfully treated with oral prostaglandin E1 analogue (limaprost).

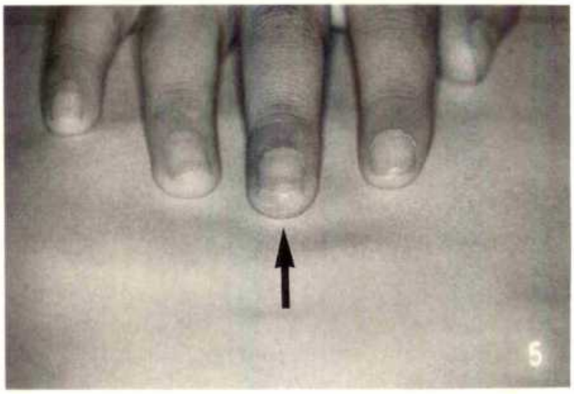
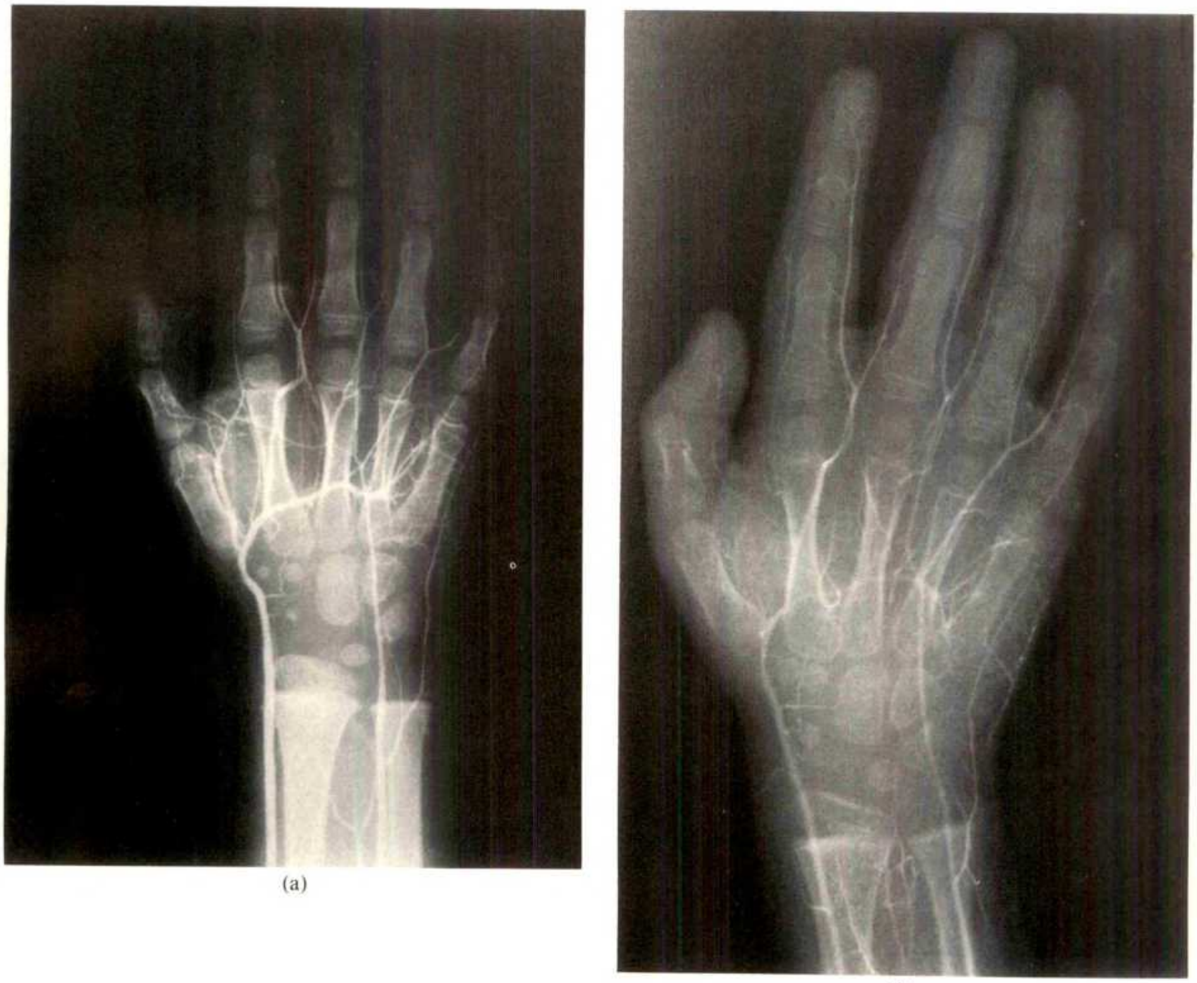


Figure 1. Epidermal ulceration revealed at the tip of the right middle finger.

Case report

A 5-year-old boy noticed the first signs of Raynaud's phenomenon after developing paleness, coldness and pain in the



(a)

(b)

Figure 2. (a) The initial right axillar arteriogram showed severe arterial spasm, and the digital arteries were not revealed. (b) Three days after administration of the limaprost, the right arteriogram showed that the relief of the vasospasm and capillary networks are visible in the tips of the fingers except for the middle finger.

fingers of both hands about 4 months before admission to our hospital. The symptoms occurred on exposure to coldness and were relieved by warming. An epidermal ulceration was also found on the tip of his right middle finger (Fig. 1). This was not associated with any other systemic abnormal findings, and his past history and family history were unremarkable. His initial investigations on admission in January 1989 revealed that his haemoglobin was 12.0 g/dl, the white blood cell count was 7200/mm^3, the platelet count was 284 000/mm^3, the erythrocyte sedimentation rate was 6 mm/h, and blood ureanitrogen was 12 mg/dl. The results of his indirect Coombs test, cold agglutinin, plasma fibrinogen concentration, and platelet aggregation rate were all in the normal range. The c-reactive protein test and plasma lupus erythematosus test (LE-test) were negative. No rheumatoid factor, antinuclear antibody or cryoglobulin were demonstrated. C$_3$ was 65/mg, C$_4$ was 25 mg/dl and testing for total haemolytic complement (CH$_{50}$) resulted in normal levels. IgG was 1190 mg/dl, IgA was 168 mg/dl, IgM 96 mg/dl and they were all within the normal limits. There was no abnormality in the urine analysis. Contrast right transfemoral axillary arteriography revealed a narrowing of the ulnar artery and the absence of digital capillary networks (Fig. 2a). The patient was successfully treated with limaprost (1.4 μg/kg per day) for 10 days, and he obtained rapid clinical and radiological improvement. He has now been free from disease since the cessation of the treatment 8 months ago.

Discussion

Raynaud's phenomenon is characterized by painful, pale and cold fingers or toes induced by functional digital vasospasm in response to coldness or emotional stimuli. In Raynaud's disease, patients show mild symptoms and excellent prognosis without associated systemic disorders (Gifford & Hines, 1957). In contrast, Raynaud's syndrome is sometimes associated with underlying systemic disorders and frequently presents haematological, serological and immunological abnormalities.

Some authors have previously described the angiographic features of patients with Raynaud's phenomenon in adult cases (Allen 1939; Laws et al, 1963; Porter et al, 1976). Allen examined the arteriograms of 22 patients with Raynaud's disease and found both diminished calibre and absence of filling-in of the digital arteries, which were considered to be in functional condition. Laws et al (1963) reported occlusive digital arterial lesions in six of the nine patients with Raynaud's disease. Porter et al (1976) revealed combined arterial spasms and organic obstructions of the digital arteries in Raynaud's syndrome and described the arterial spasms as smooth, concentric vascular attenuation. To our knowledge, there has not been any report describing the angiographic features of Raynaud's disease in childhood. In our case, in spite of the lack of evidence for collagen vascular disorders, the initial right axillar arteriogram showed narrowing of the ulnar artery and the absence of digital arteries before medication (Fig. 2a). Three days after treatment with limaprost, the angiographic features showed a considerable restoration of the distal vascular circulation coincident with the clinical improvement (Fig. 2b). These facts suggested that the initial angiographic abnormalities may be considered to be due more to the vasospasm than to the organic vascular changes in this case.

For the treatment of Raynaud's phenomenon, tolazoline, reserpine and henoxybenzamine have been employed (Guntheroth et al, 1967; Porter et al, 1976; Burns et al, 1985), but the effects of these drugs were not clear. Recently, prostaglandin (PGE_1, $PGIP_2$), which is known to work as a vasodilator and platelet-anti-aggregating agent, has been reported as being effective for the treatment of Raynaud's phenomenon (Martin et al, 1980; Burns et al, 1985). Prostaglandin is administered through a central vein or by an intra-arterial route, so the patients need to be hospitalized. CL115,347, which is a transdermally absorbed prostaglandin E_2 analogue, has been successfully employed by Belch et al (1985) and Dunger et al (1985), but the effect is not immediate. Our case was successfully treated with limaprost, and the details have been reported previously (Shono & Ikeda, 1989).

In this case all the requirements of the criteria of Raynaud's disease, described by Allen and Brown (1932), were fulfilled, except for the symptoms not having lasted for 2 years or longer. There was no evidence of systemic collagen disease in the serological, haematological and immunological investigations. Therefore it is important that this case must be carefully monitored to check for the possible appearance of collagen disease.

References

ALLEN, E. V., 1939. The peripheral arteries in Raynaud's disease. An arteriographic study of living subjects. *Proceedings of the Staff Meetings of the Mayo Clinic, 12,* 187–192.

ALLEN, E. V. & BROWN, G. E., 1932. Raynaud's disease: a critical review of minimal requisites for diagnosis. *American Journal of Medical Science, 183,* 187–200.

BELCH, J. J. F., MADHOK, R., SHAW, B., LEIBERMAN, P., STURROCK, R. D. & FORBES, C. D., 1985. Double-blind trial of CL115,347, a transdermally absorbed prostaglandin E_2 analogue, in treatment of Raynaud's phenomenon. *Lancet, ii,* 1180–1183.

BURNS, E. C., DUNGER, D. B. & DILLON, M. J., 1985. Raynaud's disease. *Archives of Disease in Childhood, 60,* 537–541.

DUNGER, D. B., DILLON, M. J., DAMMAN-WILLEMS, C. & BOWCOCK, S. A., 1985. Treatment of childhood Raynaud's disease by transdermal prostaglandin E_2 analogue. *Lancet, ii,* 50.

GIFFORD, R. W., JR. & HINES, E. A., JR., 1957. Raynaud's disease among women and girls. *Circulation, 16,* 1012–1021.

GUNTHEROTH, W. G., MORGAN, B. C., HARBINSON, J. A. & MULLINS, G. L., 1967. Raynaud's disease in children. *Circulation, 36,* 724–729.

LAWS, J. W., LILLIE, J. G. & SCOTT, J. T., 1963. Angiographic appearances in rheumatoid arthritis and other disorders. *British Journal of Radiology, 36,* 477–493.

MARTIN, M. F. R., DOWD, P. N., RING E. F. J., COOKE, E. D., DIEPPE, P. A. & KIRBY, J. D. T., 1980. Prostagrandin E_1 infusions for vascular insufficiency in progress systemic sclerosis. *Annals of the Rheumatic Diseases, 40,* 350–352.

PORTER, J. M., BARDANA, E. J., JR., BAUR, G. M., WESCHE, D. H., ANDRASCH, R. H. & RÖSCH, J., 1976. The clinical significance of Raynaud's phenomenon. *Surgery, 80,* 756–764.

SAYRE, J. W., 1973. Raynaud's disease presenting in a 5-month-old male infant. *Pediatrics, 52,* 412–415.

SHONO, T. & IKEDA, K., 1989. Rapid effect of oral limaprost in Raynaud's disease in childhood. *Lancet, i,* 908.

SINGESEN, B. A., BERNSTEIN, B. H., KRONREICH, H. K. & KING, K. K., 1977. Mixed connective tissue in childhood. *The Journal of Pediatrics, 90,* 893–900.

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Case of the month

A Chinese puzzle

By J. W. Williams, FRCS and M. C. Collins, FRCR

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(*Received March 1989*)

A 39-year-old Chinese waiter presented with a 5 week history of intermittent epigastric pain, exacerbated after eating and increasing over the 3 days preceding admission with associated retching.

Previous medical history included a vagotomy and gastro-enterostomy for duodenal ulcer many years earlier, and similar symptoms had settled with conservative management in the past.

Examination revealed abdominal distension and high-pitched bowel sounds. A plain abdominal radiograph was obtained (Fig. 1).

The patient initially settled after naso-gastric suction and intravenous fluids, but could not tolerate the re-introduction of oral fluids.

What signs are present on the plain abdominal radiograph?

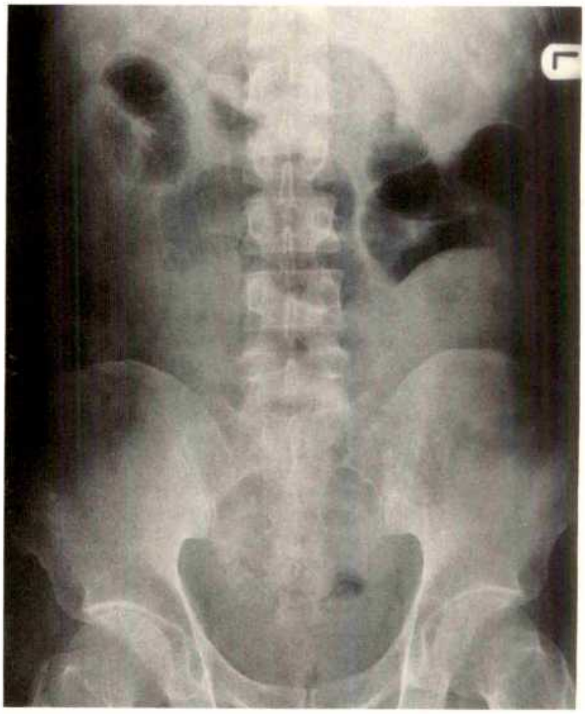
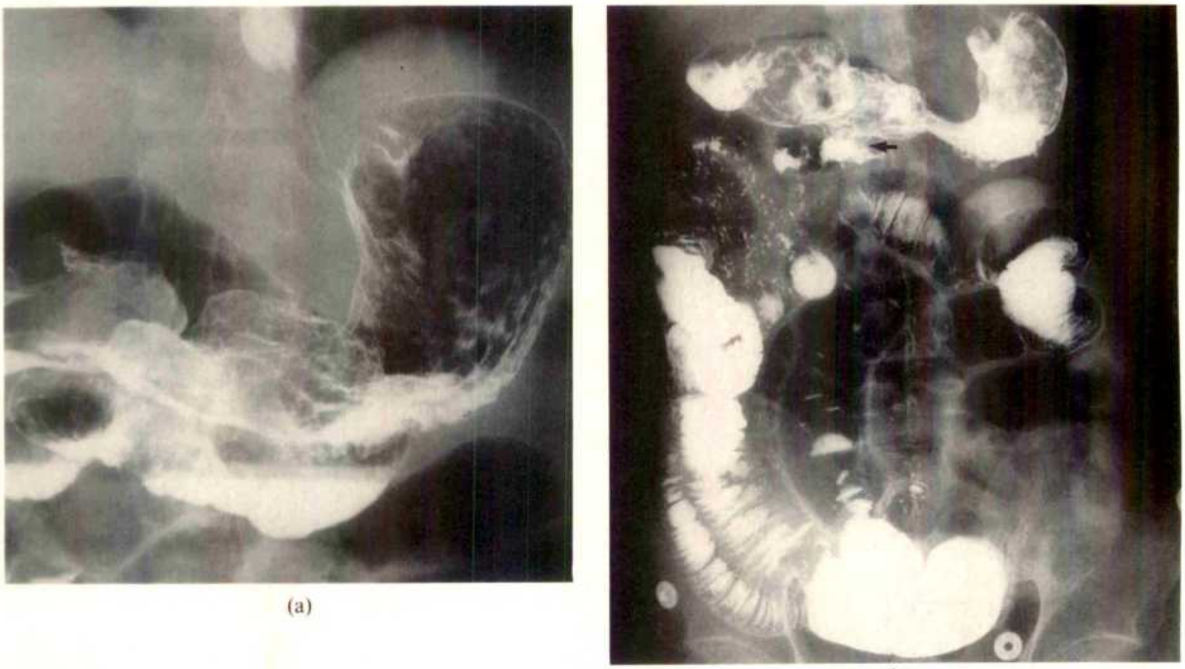


Figure 1. A plain abdominal radiograph on initial examination.



(a)

(b)

Figure 2. Radiographs from the barium meal and follow-through examination demonstrating extensive granular filling defects within the stomach. Note the gastro-enterostomy (arrow) and the small bowel obstruction.

Figure 1 shows distended small bowel loops and a granular mass within the transversely lying stomach.

A barium meal and follow-through examination was performed but the patient's condition deteriorated and he was taken to theatre for laparotomy before the procedure could be completed. Two radiographs from the examination are shown (Fig. 2). These demonstrate extensive granular filling defects, probably phytobezoars, within the stomach. The gasto-enterostomy is patent and there is small bowel obstruction.

At operation, the whole small bowel was found to be distended, because of the obstruction of the terminal ileum by a phytobezoar composed largely of rice. The stomach could not be assessed because of dense adhesions from previous surgery.

Discussion

Phytobezoars are an uncommon cause of small bowel obstruction, comprising only 2.9% of an Australian series (Vellar et al, 1986). However, a history of gastrectomy, vagotomy and drainage procedure or jejunal diverticula makes it more likely (Mir & Mir, 1973; King et al, 1985). When they are clinically suspected, gastroscopy prior to surgery will confirm the presence of any gastric bezoars and allow their endoscopic removal or proteolytic dissolution and prevent acute post-surgical recurrence.

Prophylaxis is achieved by giving dietary advice to avoid fibrous vegetables and stone-fruits to post-operative patients.

References

KING, P. M., BIRD, D. R. & EREMIN, O., 1985. Enterolith obstruction of the small bowel. *Journal of the Royal College of Surgeons of Edinburgh, 30,* 269–270.

MIR, A. M. & MIR, M. A., 1973. Phytobezoars after vagotomy with drainage or resection. *British Journal of Surgery, 60,* 846–849.

VELLAR, D. J., VELLAR, I. D., PUCIUS, R. & STEEDMAN, P. K., 1986. Phytobezoars—an overlooked cause of small bowel obstruction following vagotomy and drainage operations for duodenal ulcer. *Australian and New Zealand Journal of Surgery, 56,* 635–638.

1990, *The British Journal of Radiology*, *63*, 369

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(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Can ultrasound replace the intravenous urogram?

THE EDITOR—SIR,

We read with interest the study of Lewis-Jones et al (1989) comparing ultrasound (US) with intravenous urography (IVU) in the preliminary investigation of renal tract disease.

We have compared the two prospectively, with an almost identical protocol, in adults referred for IVU to investigate urinary tract infection (UTI) and haematuria (excluding patients with traumatic haematuria or acute loin pain).

We would concur with their comments about the need to reduce the hazards of exposure to radiation (and to contrast media) in young women, a significant proportion of patients referred for investigation of UTI. In studying 140 patients with UTI we have found US to have identical findings to IVU in 93% of cases. This increased to 96% with the addition of a single abdominal radiograph. No abnormalities were missed on US which would have altered treatment or necessitated further investigation. Our experience with the haematuria group is at variance with that of Lewis-Jones et al. We have now seen 118 patients in whom the abnormalities discovered by IVU and/or US have been evaluated by urological colleagues. We note that, of the 89 patients Lewis-Jones et al studied, US was more informative in 18 cases and IVU in three cases. They detail these US failures as three transitional cell carcinomas, two of the bladder, but did not enlarge upon the nature of the 18 IVU "failures".

In our series US proved superior to IVU in the diagnosis of bladder tumours, diagnosing all 15 lesions in the 118 patients studied; IVU failed to diagnose four bladder tumours with sizes estimated on US ranging from 5 to 21 mm. The efficacy of US in diagnosing bladder tumours is well established (Abu-Yousef et al, 1984) and has been recommended for the detection of recurrent tumours (Davies et al, 1989). We do however share the concern expressed about the ability of US to diagnose transitional cell tumours of the ureter and renal pelvis. We did not encounter any such lesions in our series. They are rare by comparison with bladder tumours but, in the case of ureteric tumours, three-quarters present with non-function or upper tract dilatation on IVU (Williams & Mitchell, 1973a,b); US may be expected to detect such abnormalities.

Overall in our series of patients with haematuria, the majority of whom were referred from local general practitioners, US findings agreed with those of IVU in 94% of cases and yielded more information than IVU over and above its advantages in imaging the bladder. The main failure of US was in diagnosing small urinary calculi but the addition of a single abdominal radiograph corrected this deficiency.

The decision to move from IVU to US as the primary imaging study will be influenced as much by the needs of the referring clinician as the overall accuracies of two techniques. We would agree that few if any urologists would consider the advantage of US in diagnosing early bladder tumours to outweigh the smaller risk of missing an early upper tract transitional cell tumour, particularly when cystoscopy is planned. For the general practitioner, the choice is not so easy. Increasingly patients are referred for the investigation of dipstick haematuria. As a primary imaging study in these patients we believe US offers significant advantages over IVU when progression to cystoscopy would be by no means universal. In times of cost benefit analysis US may also be recommended (Corwin & Silverstein, 1988).

Yours, etc.

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References

ABU-YOUSEF, M. M., NARAYANA, A. S., FRANKEN, E. A. & BROWN, R. C., 1984. Urinary bladder tumors studied by cystosonography. *Radiology*, *153*, 223–226.

CORWIN, H. L. & SILVERSTEIN, M. D., 1988. The diagnosis of neoplasia in patients with asymptomatic microscopic hematuria: a decision analysis. *Journal of Urology*, *139*, 1002–1006.

DAVIES, A. H., CRANSTON, D., MEAGHER, T. & FELLOWS, G. J., 1989. Detection of recurrent bladder tumours by transrectal and abdominal ultrasound compared with cystoscopy. *British Journal of Urology*, *64*, 409–411.

LEWIS-JONES, H. G., LAMB, G. H. R. & HUGHES, P. L., 1989. Can ultrasound replace the intravenous urogram in preliminary investigation of renal tract disease? A prospective study. *British Journal of Radiology*, *62*, 977–980.

WILLIAMS, C. B. & MITCHELL, J. P., 1973a. Carcinoma of the renal pelvis—a review of 43 cases. *British Journal of Urology*, *45*, 370–376.

——1973b. Carcinoma of the ureter—a review of 54 cases. *British Journal of Urology*, *45*, 377–387.

1990, *The British Journal of Radiology*, *63*, 370–372

Proceedings of The British Institute of Radiology

What shall we do about osteoporosis?

Abstracts of papers presented at a joint all-day meeting organized by the BIR and the National Osteoporosis Society held at the Windeyer Building, Middlesex Hospital, Cleveland Street, London W1 on Wednesday, 22 November 1989

Chairman: Professor P. J. Ell

What is osteoporosis and why is it a major disease? by I. Fogelman
The physics of bone density measurement, by I. Cullum. Abstract not received
Single and dual γ photon absorptiometry: relative merits, by R. Valkema
The role of quantitative computed X-ray tomography, by J. Adams
A comparison of dual energy absorptiometry, by M. Fischer and B. Kempers
First data on a UK normal range for dual energy X-ray absorptiometry, by M. L. Hall, J. Heavens, I. D. Cullum and P. J. Ell
Hormone treatment—efficacy and safety, by H. Jacobs. Abstract not received
Fracture prediction in osteoporosis, by A. Horsman
Role of DEXA in non-osteoporotic bone disease, by L. Rosenthall
Advances in the investigation and treatment of established osteoporosis, by P. Meunier. Abstract not received

What is osteoporosis and why is it a major disease?

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Osteoporosis is a disease in which there is too little bone and individuals are at increased risk of fracture, often without significant trauma. The clinically most relevant fractures are those of the forearm, spine and hip. Fracture of the hip has received the most attention as, in addition to the high morbidity, the need for hospital admission and escalating financial costs, there is significant mortality of around 20% as a result of related complications. However, fracture of the spine should not be forgotten, as this tends to affect a relatively younger group of women who may have to look forward to many years of chronic discomfort and increasing deformity. It is of concern that the incidence of osteoporotic fracture has been found to be increasing in some countries, *e.g.* Scandanavia and the United Kingdom. The cause for this is not apparent. Nevertheless while individuals are living longer it would appear that there is a deterioration in skeletal quality from one generation to the next. Hospital costs are rising, individuals are living longer and the incidence of osteoporosis appears to be on the increase. The problems relating to osteoporosis can no longer be ignored and if positive steps are not taken to tackle them then, leaving aside the issues of morbidity and mortality, the financial implications are frightening. In the United States it has been suggested that the cost of hip fractures may eventually bankrupt the health services!

Single and dual γ photon absorptiometry: relative merits

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Single photon absorptiometry (SPA) and dual photon absorptiometry (DPA) have gained widespread acceptance as noninvasive techniques to measure bone mineral content (BMC). Since reduced bone mass is one of the most important risk factors for fractures, DPA and SPA are used to select patients who need preventive measures or therapy, as well as to monitor the effects of the installed therapy. With SPA, only measurements at the appendicular skeleton are feasible. Although there is a significant correlation between BMC at the forearm and the spine or hips, this correlation is not close enough to predict axial BMC from appendicular measurements. Furthermore, changes in BMC at the midradius seem to correlate not at all with changes in BMC at the lumbar spine. With DPA the axial BMC can be measured, in particular at the vertebral column and hips, which are the most important sites for osteoporotic fractures. The reported precision and accuracy of DPA are approximately 1–3% under optimal conditions, but in everyday clinical practice errors twice as large are likely. The accuracy and precision errors of DPA will be worse in patients with low bone mass, scoliosis, osteophytes, aortic calcifications and/or inhomogeneous distribution of paravertebral fat. Another major cause of error is the relatively low yield of photons emitted from the 153-Gd source. As a result, the spatial resolution of DPA is less than optimal with difficulties in selection of the region of interest. The changes in bone mineral mass range from less than 1% to approximately 3% per year in most cases and therefore, the precision of DPA is insufficient for reliable follow-up of individual patients. The recently introduced technique of dual energy X-ray absorptiometry (DEXA) is based on the same principles as DPA, but instead of a radioactive source it uses an X-ray tube. Its precision is better than the precision of DPA, so DEXA may fulfil the promise that DPA has made.

The role of quantitative computed tomography

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Quantitative computed tomography (QCT) is now established as an important non-invasive technique of bone mass measurement. It is applied principally to the spine, but measurements have also been made in peripheral sites. Single sections are performed through the middle of vertebrae generally T_{12} to L_3, using a low dose technique (80 kV, 70 mA, 2s). This results in a radiation dose of 1.75–2.0 mGy for each examination (1/5 of the dose of a lateral lumbar radiograph). To correct for scanner instability or beam hardening, scanning is performed with a bone equivalent calibration phantom to convert attenuation value for the region of interest (ROI) into mineral equivalents (mg/ml). Original phantoms contained K_2HPO_4 solutions, but because these showed some change with time, solid hydroxyapatite phantoms are now being developed. For any measurement technique to be clinically useful, high precision is a prerequisite. Careful attention to scanning details and patient positioning is essential. Automation of scan plane and ROI selection results in a precision of 1–2% for spinal QCT. Measurements from different scanners may not be identical and in longitudinal studies it is imperative that the calibration phantom is not changed. Marrow fat will cause some underestimation of mineral content of trabecular bone. Accuracy can be improved by using dual energy QCT, but with reduction in precision, increase in radiation dose and considerable technical effort. Monochromatic isotope CT scanners have been developed for peripheral skeletal sites (radius, tibia). In common with other non-invasive techniques (SPA, DPA, DPX) QCT can measure integral (cortical and trabecular) bone. However, QCT is unique in allowing separate estimations of trabecular and cortical bone. Since trabecular bone is some eight fold more active metabolically than cortical bone, QCT is the most sensitive method for monitoring changes in trabecular bone in response to treatment and serially in patients with metabolic bone disease. It can detect age-related changes in bone mass in the normal population, and the accelerated loss which occurs at the menopause. Fractures are likely with QCT values below 110 mg/ml and inevitable below 60 mg/ml ("fracture threshold"). Although, as with other techniques, in older populations there is an overlap of QCT values in osteoporotics and normal subjects of the same age.

Inter-unit variation of bone densitometry systems

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The different bone mineral content (BMC) of European and American population has been discussed recently. The aim of this study was to compare the intra- and inter-unit variation of bone densitometers (BD) of different companies using an animal spine as a phantom and to build a phantom for cross calibration. Six vertebras of a pig were encapsulated in 16 cm of soft-tissue-equivalent material. Three vertebras of this phantom were measured with BDs using either radionuclide sources ($n = 6$) or X-ray tubes ($n = 3$). In each series the phantom was measured several times. To exclude the inaccuracy of BDs caused by varied soft-tissue compositions, the BMC of the phantom was measured with different overlying tissue (water and/or fat). Whereas the inter-unit variation was as much as 20%, the intra-unit variations were less than 1% in all systems but two, in which a coefficient of variation of 5% was observed. These two BDs were more than 5 years old. Overlying the phantom with water (4 and 8 cm) and/or fat (3.5 and 7 cm), different results were observed. Some BDs showed variations of basal values of about 8–10%, others were not influenced. During a long-term measurement of the phantom with two BDs, the coefficient of variation was less than 2%. The inter-unit variation of bone densitometry systems may be a result of various calibrations, whereas the under- or overestimation of BMC, depending on different overlying soft tissue, may be caused by different software algorithms. Because of these differences, a comparison of BMC values measured by different BDs is problematic. We therefore built a phantom with cylindric bodies with different hydroxyapatite content for cross calibration of BDs. By using such phantoms, a standardization of BDs should be possible.

First data on a UK normal range for dual energy X-ray absorptiometry

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Dual energy X-ray absorptiometry (DEXA) is a new technique for the measurement of bone mineral density. The results given are in g/cm^2 and have a different value from previous dual energy methods. The normal range of bone density for US subjects is supplied with the machine (Hologic 1000); however, it has been shown that the results vary between populations. It is for these reasons that we studied the range of bone density in 207 British women from the ages of 4 to 70. Strict inclusion and exclusion criteria were applied and the resulting mean and standard deviations compared with the US data. The UK results are shown below (Table 1). From our cross sectional data there is no obvious peak in bone density, longitudinal studies will be needed to confirm the timing of any peak bone mass. Bone density values decreased after the menopause and the mean result was significantly different from any premenopausal age group. Comparison with the US range is adequate but a specific UK range from more subjects is preferable.

Table I. The range of bone density: UK results

Age	Mean bone mineral density (g/cm^2)	Standard deviation
20–29	1.053	0.085
30–39	1.058	0.098
40–49	1.063	0.134
50–59	0.923	0.128
60–69	0.821	0.121

Fracture prediction in osteoporosis

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By means of a stochastic model that simulated falls and bone loss from the proximal femur in an ageing cohort, it was shown that in women, up to the age of about 70, the risk of fracture of the hip following a fall increases exponentially with decreasing bone mineral density (BMD) in the femoral neck. To account for the continuing increase in the age-specific incidence of hip fracture in higher age groups, it was necessary to include in the model an age-related risk multiplier that was independent of BMD and rose rapidly over the age of 70. The proportion of all hip fractures occurring in an ageing female cohort was estimated in relation to individual membership of groups classified by BMD at maturity and/or rate of decrease of BMD in middle age. The model predicted that about 60% of all fractures occur in those 25% of women who at maturity have the lowest values of BMD. Estimates of lifetime risk of hip fracture based on an individual's measured value of BMD at any age (A) and life expectancy (L) were also calculated. For any particular values of A and L, the lifetime risk was shown to rise rapidly as BMD decreases. Such risks could be modified by long-term therapy which affected the course of age-related bone loss and/or the way in which the risk of falls increased with age in the individual. The likely reduction in fracture incidence resulting from large-scale prophylaxis was evaluated taking into account its possible effects on bone loss and falls.

Role of DEXA in non-osteoporotic bone disease

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A review was undertaken of all patients seen at the Metabolic Bone Unit during the last year. An analysis of the non-osteoporotic metabolic bone disorders yielded the following results. Renal dialysis: 48 patients on dialysis for a mean (sd) of 6.5 (5.2) years had a mean (sd) age-matched spinal BMD of 101 (17)%, but 8/48 (17%) patients had BMDs exceeding 2 standard deviations, which is a significant occurrence of sclerosis. The mean (sd) BMD of the hips in 16 patients was 99.3 (20.8)%, but 4/16 (25%) patients had BMDs in excess of 2 standard deviations. Anorexia nervosa: the mean (sd) age-matched spinal BMD of 16 women (mean age 32 years) was 78.9 (11.4)%, which is more than 2 standard deviations below normal. Hypogonadism: 15 male patients of mean (sd) age 38 (13) years registered a mean (sd) spinal BMD of 72.2 (14.4)%, more than 2 standard deviations below normal. Similarly, hypogonadism in 10 female patients with a mean (sd) age of 27 (6) years had a mean (sd) spinal BMD of 78.6 (14.4)%: significantly low. X-linked hypophosphatemia (hyperphosphaturia): there were 14 patients in this catagory and all had been treated for many years with vitamin D and phosphates. The mean (sd) spinal BMD was 131 (31)%, 3 standard deviations above normal. This intense sclerosis was not always reflected in the hip BMDs in the few determinations that were done. Idiopathic juvenile osteoporosis: four female patients, aged from 10 to 14 years, had a mean spinal BMD of 65% of that predicted for their age and weight. Osteogenesis imperfecta: five patients, one male and four female, aged from 10 to 15 years, yielded a mean spinal BMD of 67% of that expected for their age and weight.

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Proceedings of the British Institute of Radiology

Radiation protection: sense or nonsense?

Abstracts of papers presented at an all-day meeting of the BIR held at the Windeyer Building, Middlesex Hospital, Cleveland Street, London W1 on Wednesday, 13 December 1989

Chairman: Dr R. J. Berry

Cancer in Swedish iron miners; a nearly complete follow-up study, by E. Radford
Radon exposure, marrow and fetal dose, and leukaemia, by D. L. Henshaw
Incidence of leukaemia in young people in the vicinity of Hinkley Point nuclear power station, by P. Ewings, C. Bowie, M. J. Phillips and S. A. N. Johnson
Occupational exposure and the central index of dose information, by G. M. Kendall
Medical diagnostic exposure, by J. G. B. Russell
Medical therapeutic exposure, by M. J. Day
The standard man in diagnostic radiology dosimetry, by B. A. Lindskoug
Reduction of dose due to radon in housing, by S. J. Wozniak
Reduction of occupational dose, by R. J. Berry
Reduction of dose in diagnosis, by B. F. Wall
Radiation protection—the environmental view, by P. Green

Cancer in Swedish iron miners; a nearly complete follow-up study

Edward P. Radford
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We have obtained mortality data for 1415 Swedish iron miners who worked underground and were exposed to relatively low concentrations of radon daughters. The cohorts studied were men born between 1880 and 1919 who were alive on January 1st 1930. Control populations have been the Swedish national population and men from the nearby communities from the same birth years. Follow-up has now been completed up to 1986, at which time only 30% of the miners were still alive. Thus this study population is epidemiologically the most complete in the world of any group studied prospectively. Comparison of the two control populations shows that causes of death differed significantly for the local population compared to Swedish national rates. For example, a stomach cancer excess among miners is found to be present among local controls as well. Seventy-three deaths from lung cancer have been observed among miners compared with 17.6 expected from community data. The absolute excess lung cancer risk for cigarette smokers is 1.66 times that for non-smokers, but the relative risk coefficient for non-smokers is four times that for smokers. The excess relative risk for lung cancer has continued unchanged even though all men have retired from underground work since 1978. A significant excess of multiple myeloma has been observed among the miners in recent follow-up years, and a more than three-fold excess of liver and gall bladder cancers has also been found. The evidence suggests that these last two observations may be related to occupational radon exposure.

Radon exposure, marrow and fetal dose, and leukaemia

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Recent calculations of dose from inhaled radon to bone marrow and the fetus yield values considerably higher than that assumed by ICRP. By taking into account the presence of fat in marrow, in which radon is 16 times more soluble than in blood, and the contribution from inhaled excess radon daughters in room air, we calculate, for a radon exposure of 20 Bq/m^3, marrow doses of 123 μSv/y and 129 μSv/y^4 for the adult and a child aged 10, respectively. For the fetus the doses are in the range 28–49 μSv/y. For radon exposures of 400 Bq/m^3, the respective doses are 2600, 2620 and 540–1120 μSv/y. These results suggest that domestic radon exposure could be a causative factor in the induction of leukaemia. We have therefore looked for an association between radon exposure and leukaemia incidence in particular but of other cancers in general. International incidence of myeloid leukaemia, cancer of the kidney, melanoma and certain childhood cancers all show significant correlation with radon exposure in the home. For myeloid leukaemia analysis suggests that overall in the UK between 5% and 10% of incidence may be attributed to radon. In Cornwall, where radon levels are higher, we estimate that at least 17% of myeloid leukaemia is caused by radon.

Incidence of leukaemia in young people in the vicinity of Hinkley Point nuclear power station

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Data reported in Ewings et al (1989) are discussed. Cancer registry data are used to examine the incidence of leukaemia and lymphoma in persons aged under 25 years living in the vicinity of Hinkley Point nuclear power station. The 19 cases occurring in a predefined area around Hinkley Point during 1964–1986 are 82% more than expected from national rates (95% confidence interval 10% to 185%). However, Somerset as a whole has high rates compared to the national average, and the area around Hinkley Point has only 54% more cases than the Somerset average. This figure is not statistically significantly higher, so the high rate around Hinkley Point may simply be reflecting the generally high rate in the Somerset area. Temporal patterns are examined using standard 5 year intervals. Particularly high rates are revealed around Hinkley Point for the 10 years following commissioning of the station (1964–1973), when rates in the rest of Somerset were similar to the national average. In particular, the nine cases occurring in the 5 year period 1969–1973 is about four times the number expected from national rates. After 1973, the rates around Hinkley Point are fairly low. The pattern of leukaemia cases observed around Hinkley Point cannot readily be explained. In common with results for other nuclear installations, radioactive emissions do not provide a plausible explanation according to current understanding of exposure, dose/risk relationships, etc. The possibility that the current models are flawed is examined. Other possibilities recently suggested, namely the implication of viral transmission resulting from the influx of a large workforce into a susceptible community, and geographical factors common to installation sites, are discussed.

Reference

EWINGS, P. D., BOWIE, C., PHILLIPS, M. J. & JOHNSON, S. A. N., 1989. Incidence of leukaemia in young people in the vicinity of Hinkley Point nuclear power station, 1959–86. *British Medical Journal, 299*, 289–293.

Occupational exposure and the Central Index of Dose Information

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Optimized control of the radiation exposure of workers requires a knowledge of the individual's full radiation dose history. There are obvious difficulties in assembling comprehensive dose histories for workers who change employment and a number of countries have set up dose depositories to make this process more reliable. The UK scheme is known as the Central Index of Dose Information (CIDI). It is operated on behalf of the Health and Safety Executive by the National Radiological Protection Board. In order to keep costs to a minimum CIDI operates by exchanging data with Approved Dosimetry Services in the form of closely defined computer compatible records. While the use of computerized data transfer makes for more economical running it is potentially dangerous since the data are not scanned by human intelligence. Special data vetting software has been written for quality assurance. Special attention is given to ensuring that successive employments of an individual are brought together even if the name or National Insurance number may have been mis-reported. Occupational exposure to ionizing radiation in the UK is covered by the 1985 Ionizing Radiations Regulations. About 40 000 individuals are radiation workers within the sense of these regulations. It is this group which will be covered by the CIDI. However, personal monitoring is not restricted to these "classified workers" and many more individuals are monitored in order to provide reassurance. When the variation of mean dose to a group of workers with time is explored it is generally found that there is a downward trend, *i.e.* doses appear to be falling. However, it is often difficult to be sure that this does not arise through the "dilution" of a group of genuine radiation workers by individuals receiving low dose. Evidence from one large Personal Monitoring Service has now been found to suggest that this is not the case and that the reduction in mean dose with time is genuine. There is also interest in the variation in mean dose between different occupational groups. The workers receiving the largest doses work in non-coal mines, in 1987 the mean dose was reported to be 14 mSv, higher by a factor of three than the next largest group.

Radiation protection: sense or nonsense medical diagnostic exposure

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In the United Kingdom the average population radiation dose for the average diagnostic room is 4 man Sv. This varies from room to room. A busy room devoted mainly to chest work would give only about 1 man Sv per year; a busy barium room is likely to give 10 man Sv per year or more. The new risk factors for a population with the age distribution of patients is likely to indicate a risk of fatal cancer induction at a rate of 3% per Sv. Adding the risk of non-fatal cancer and genetic injury will give a risk of serious radiogenic injury at a rate of 4% per Sv. With an annual United Kingdom population dose from diagnostic radiography of 16 000 man Sv per year this indicates about 640 serious radiogenic injuries will occur each year, most of them fatal cancers from diagnostic radiography. Using the new risk factors and using established methods of assessing the value of harm a reasonable figure to spend to avert 1 man Sv is £20 000. The cost of saving radiation in a diagnostic department is trivial compared to this value. Many of the methods which will be discussed by Mr Wall cost nothing. For instance, the careful use of the lead shutters, the avoidance in an examination of views which add no information and not doing unnecessary examinations are obvious examples in this category. The cost of other methods of saving radiation, *e.g.* using rare earth screens or low attenuation components in the apparatus which lie in the primary beam, are also highly cost effective.

Medical therapeutic exposure

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Radiotherapeutic exposure is unique in that the object is to bring about a definite and beneficial radiobiological effect. Consequently the general principles of radiation protection are only marginally applicable and it is difficult to make meaningful comparisons with other types of exposure. The local tumour dose is relatively high (*e.g.* 50 Gy) and the whole-body average dose is typically a few gray. About 1 in 10 of the population receive radiotherapy. Patients are usually elderly and have reduced life-expectancy and fertility. The contribution to the GSD is only marginal. Although radiotherapeutic exposure must be justified by the expectation of net benefit to the patient, the system of dose limitation and the concept of acceptable risk are not applicable. The dosage to normal tissues should indeed be minimized, but in the absence of an alternative to the effective dose equivalent it is difficult to apply the ALARA principle. In radiotherapy, optimization involves balancing cure-rate against the risk of high-dose effects such as necrosis, with virtually no cost implications. The optimal practice of radiotherapy requires reliable dosimetry, good anatomical localization, individual planning and accurate administration of the treatment. By contrast, optimization of radiation protection involves off-setting the cost of protective measures against reduction of collective dose: essentially a matter for society as a whole. The risk estimates used in radiation protection have some limited application to the incidence of radiation-induced tumours outside the main treatment zone. Methods for protection against occupational exposure in external beam radiotherapy and brachytherapy are discussed briefly.

The standard man in diagnostic radiology dosimetry

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One problem with the ICRP standard man is that less than one quarter of the human population on this planet corresponds with the Caucasian dimensions stipulated. Moreover, even the average weight of a limited European population rarely agrees with the expected 70 kg. Infants, children, adolescents or obese adults unbalance the distribution. Similar problems exist in using Monte Carlo tables computed for the standard man, no limited population will agree. The same problem occurs when comparing two samples of patient examinations. The populations equal neither in weight, nor height, nor constitution. This is the major reason for the extreme deviation of absorbed dose given to patients during diagnostic radiology examinations. A close relation is found between the total energy imparted during radiology examinations of the trunk and the equivalent cylindrical diameter (De) of the patient body. Exponential functions are created by linear regression in logarithmic space. Coordinate transformations reduce data to a base-line defined by the ICRP standard man with De = 22.9 cm. Organ dose and effective dose equivalent are computed from the reduced data. By standardizing data in accordance with exponential functions using the equivalent diameter as the independent variable, the deviation is reduced according to the following table:

Examination	Relative reduction (%)		
	Mean dose	SD	High/low ratio
Lumbar spine	15	51	76
Thoracic spine	12	19	22
Urography	28	62	94
Colon	13	5	85
Chest	12	41	74
Heart and lung	12	39	90

Improved diagnostic precision and reduced total energy imparted to individuals (film exposure plus radiography), which includes improved image quality and reduced dose, are the parameters that should be optimized for a mutual technical and methodical improvement and assessment of organ dose for future classification of detrimental effects.

Reduction of dose due to radon in housing

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The Building Research Establishment is undertaking work in existing housing to determine appropriate remedial options for elevated indoor radon levels. Initial studies have been undertaken in houses identified by NRPB and having the highest concentrations. Most of these are located in Devon and Cornwall. Work in new housing is also in progress to determine appropriate protection or remedial treatments. A feature of domestic radon exposure in the UK is that little of the collective effective dose equivalent occurs in "high level" houses. Thus, the prospects for cost-effective dose avoidance may be limited. The UK position is reviewed, based on NRPB estimates of the number of houses having annual average radon gas concentrations above both $400\ \text{Bq/m}^3$ and $200\ \text{Bq/m}^3$, the latter being the lower of the two "action levels" suggested for the UK, and close to the USA threshold of $150\ \text{Bq/m}^3$. It is shown that, whilst the prospects for technical remediation are good, the realistic potential for premature death avoidance in houses above either action level is certainly less than 100 persons per year, and probably less than 40 per year, including 10 non-smokers. This is compared with an annual total of nearly 40 000 lung cancer deaths, including 2000 calculated to be owing in part to domestic radon exposure and including 500 non-smokers.

Reduction of occupational dose

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Over the past decade the requirement to keep doses received occupationally "as low as reasonably achievable", as laid down in ICRP Publication 26 (1977) has effectively halved the average annual dose to workers at British Nuclear Fuels, Sellafield reprocessing plant. Reduction in collective dose has been harder to achieve. In the electricity supply industry, average worker doses have decreased, although less dramatically, both in the UK and in other countries, and the record of the United Kingdom is good in the reduction of both individual and collective occupational dose across the whole of the nuclear industry. Better management of maintenance and refurbishment tasks has achieved significant reductions in worker exposure, but at an economic cost which exceeds the notional value of a man-sievert saved. For reductions in dose to the public from the nuclear industry, the disproportion between the cost and the notional value of a man-sievert saved may be as high as $10^5 : 1$. The recommendation by NRPB, that dose limits for occupationally exposed people should be set by averaging over a period up to 10 years, is supported strongly; excessively restrictive annual dose limits do not in practice reduce average occupational exposures and may result in actual increases in collective occupational dose. Examples are given of the way in which the cost of reductions in occupational radiation exposure are managed in BNFL by delegation of financial authority to appropriate levels of management.

Reduction of dose in diagnosis

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The fact that medical X rays contribute about 90% of the total collective dose to the population of the UK from all man-made sources, testifies to the enormous benefit to the health of the nation that is attributed to this use of radiation by both the medical profession and the public. The overall effect of medical X rays is undoubtedly seen as an improvement in health care and to be of benefit, dose reduction in radiodiagnosis must be aimed only at *unnecessary* medical exposures. It is essentially this unbeneficial component of the collective medical dose that should be more properly compared with other sources of population exposure when assessing the relative urgency of directing resources at reducing them, since no other source of radiation exposure can claim to have the direct health benefit potential of medical radiology. This paper attempts to assess the extent of unnecessary medical exposures in the UK, which turns out to be substantial. Possibly as much as one third of the collective dose from medical X rays could be avoided without jeopardizing patient care. It goes on to determine the cost and effectiveness of a number of dose reduction methods. Many simple changes in *procedure* cost nothing while some dose saving improvements in *equipment*, like changing over to rare-earth screens, are also found to be extremely cost-effective and yet surprisingly have not received anything like universal adoption in the NHS. One reason for the low priority given to radiation protection in the health service may be the competition from other more effective methods of health care for the same limited resources. A rough comparison was made of the cost-effectiveness of some radiation protection options and a range of common medical procedures, in terms of the cost per quality adjusted life year saved (£/QALY). It indicated that even relatively expensive patient protection measures (like carbon fibre table tops) appear to compete favourably with a number of medical procedures that already consume large amounts of health service resources.

Radiation Protection: the environmental view

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For many years environmental groups have claimed that radiological protection standards underestimated the risk from exposure to ionizing radiation. A claim rejected by the nuclear industry and its regulatory authorities as unsupported by the scientific evidence. For such organizations the emphasis was on the ALARA principle (all doses must be kept as low as reasonably achievable) as the most effective way to reduce exposures, not changes in the dose limits. The latest evidence from the Radiation Effects Research Foundation in Japan has changed this. It is now accepted that risk estimates will rise and dose limits will have to be reduced. The question is when should they be changed and by how much? Following the International Commission on Radiological Protection's (ICRP) 1987 Statement that the new evidence was not sufficient to warrant an immediate change in its dose limits, the UK National Radiological Protection Board (NRPB) stated interim guidance was necessary. They recommended a three-fold increase in the risk estimates for radiological protection purposes. Since then, at the Hinkley Point 'C' Public Inquiry, they have recommended further increases in these risk estimates. These estimates differ from those suggested by Friends of the Earth only in terms of the Dose Rate Effectiveness Factor used. Next year, the ICRP are finally expected to publish their new recommendations. The ICRP's current system of radiological protection is based around three main features: (1) justification, (2) ALARA and (3) dose limits. This talk discusses this system in light of the increases in risk, and considers, from an environmental perspective, what changes should be made.

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List of sections

	Page
Paediatric and small parts	377
Veterinary ultrasound	380
Abdominal ultrasound	382
Obstetric ultrasound	385
Gynaecological ultrasound	388
Physics and instrumentation	390
Orthopaedic teach-in	393
Cardiovascular ultrasound	395
Posters	398

Paediatric and small parts

Chairmen: W. Lees and J. Greene

Ultrasound in the diagnosis and follow-up of neonatal renal vein thrombosis, by R. J. Davies, C. Dicks-Mireaux, and R. De Bruyn
Ultrasound in the assessment of cholestatic jaundice in the young child, by R. J. Arthur
Suspected spinal dysraphism in infancy—The role of high resolution ultrasound, by T. Jaspan and C. I. Rothwell
Ultrasound of the cold thyroid nodule, by I. Stewart, A. Ahuja, W. Tang and C. Metreweli
The use of ultrasound in the assessment of abnormalities detected by mammography screening, by M. J. Michell, R. Given-Wilson and H. B. Numerley
Ultrasound diagnosis of bilateral varicocoele and its clinical significance, by O. Nicholas, L. Berger, N. Amso and R. W. Shaw
The use of real-time ultrasound in the management of scrotal trauma, by C. A. Lewis and M. J. Michell
Transrectal ultrasound in the investigation of haemospermia, by R. J. Etherington, R. Clements, G. J. Griffiths and W. B. Peeling
Sonographic detection of foreign bodies of the extremities, by B. Banerjee and R. K. Das

Ultrasound in the diagnosis and follow-up of neonatal renal vein thrombosis

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The ultrasound findings in ten neonates with renal vein thrombosis presenting to the Hospital for Sick Children between 1984 and 1989 were reviewed in order to assess the value of ultrasound in the diagnosis and subsequent management of this condition. The range of ultrasound appearances, and their frequency, in this condition are described. The outcome in terms of renal appearances and function is also examined. At presentation, equal numbers of patients had unilateral and bilateral involvement. The affected kidney was enlarged in 40% of cases, and showed increased echogenicity in 70%. Loss of cortico-medullary differentiation occurred in 50%. An associated adrenal haemorrhage was seen in 20%, whilst extension of the thrombus into the inferior vena cava (IVC) occurred in only 10% of patients. The diagnosis was sometimes difficult, and acute tubular necrosis was the most common condition causing confusion. The echographic differentiating features are discussed. The final outcome was similar in most cases, consisting of a small, scarred kidney with an average differential function of 29% as measured by isotope DMSA scan. Chronic renal failure was seen in only one patient with bilateral involvement. Conclusion: ultrasound is a valuable, non-invasive means of imaging renal vein thrombosis and its associated complications of adrenal haemorrhage and IVC thrombosis. The typical findings at diagnosis and follow-up are presented, and the differential diagnosis discussed.

Ultrasound in the assessment of cholestatic jaundice in the young child

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The ultrasound examination is often the keystone in the assessment of cholestatic jaundice in the adult, particularly in distinguishing obstructive from non-obstructive causes. In contrast, despite considerable advances in technology, diagnostic difficulty persists for both the radiologist and the paediatric surgeon in the evaluation of conjugated hyperbilirubinaemia in the young, especially during early infancy. The records of 92 children, aged less than 2 years, who presented with cholestatic jaundice have been reviewed with a view to determining the value of the ultrasound examination in their assessment. The final diagnoses included 37 infants with extrahepatic biliary atresia (EHBA), 20 with neonatal hepatitis, 7 related to parenteral nutrition, 5 with biliary hypoplasia, 5 with cholelithiasis, 4 infants with choledochal cysts and 3 infants with αI antitrypsin deficiency. A number of other aetiologies accounted for the other 11 patients. The ultrasound findings in these children are described and attention drawn to the lack of bile duct dilatation in EHBA, the commonest "surgical" cause of jaundice in the infant. This makes differentiation from neonatal hepatitis, by ultrasound alone, almost impossible. The limitations and pitfalls of biliary tract ultrasound in early infancy are discussed.

Suspected spinal dysraphism in infancy — the role of high resolution ultrasound

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The neonatal and early infant spine is well suited to ultrasound examination owing to the immature ossification of the posterior neural arches at this age. Although widely employed in North America, there is relatively little use of ultrasound in the investigation of spinal dysraphism in the UK. We present our initial findings in 24 patients with suspected spinal dysraphism. All examinations were performed on an Acuson 128 system employing a 5 or 7 MHz linear array probe. Twelve patients with dorsal lumbosacral cutaneous pits were referred for the exclusion of an associated dysraphic anomaly. Dermal sinus tracks were found in three patients, passing to the spinal canal in two and into the thecal sac in one (associated with an epidermoid cyst), confirmed at surgery in each case. Spina bifida cystica lesions were studied in four patients, three with lipomyelomeningocoeles and one with a primarily repaired myelomeningocoele. Spinal lipomas were found in three patients, diastematomyelia in two and there were single cases of sacral agenesis and a low tethered cord. Confirmatory CT assisted myelography (CTM) was obtained in six cases, MRI in four cases and surgical findings obtained in nine patients. There was one false positive ultrasound examination (suspected lumber diastematomyelia not confirmed by CTM). Ultrasound correctly identified hydrosyrinxs in two cases (confirmed by MRI) which were not shown by CTM. The ultrasound findings facilitated performance of CTM by indicating the presence and location of neural tissue within cystic lesions. We have found spinal ultrasound to be a very useful adjunct to the investigation of spinal dysraphism and, in certain circumstances, it can be used as the definitive examination. The avoidance of ionizing radiation and the non-invasive nature of the technique are of additional benefit.

Ultrasound of the cold thyroid nodule

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Most texts on thyroid imaging give pre-eminence to scintigraphy. Ultrasound is relegated to establishing whether the lesion is "solid" or "cystic". Unfortunately the wide spectrum of appearances of the thyroid shows that this simplistic division is impractical. We have reviewed 100 cases with cold nodules. The ultrasound findings were:

Solitary cold nodules		Two or more cold nodules	
Adenomas	44%	Multinodular thyroid	44%
Spontaneous haemorrhage	12%	Cystadenomas	20%
Cystadenomas	12%	Spontaneous haemorrhage	16%
Thyrotoxic	12%	Adenomas	12%
Multinodular thyroid	9%	Carcinoma	8%
Carcinoma	6%		
Nothing	6%		

Conclusion: Ultrasound is more eloquent.

The use of ultrasound in the assessment of abnormalities detected by mammography screening

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Following implementation of the Forrest Report, up to 10% of women who are screened may be recalled for further assessment because of an abnormal mammogram. The methods available for the further evaluation of these women are further mammography including magnification and localized compression views, clinical examination and ultrasound. Breast ultrasound has previously been shown to distinguish cystic from solid breast lesions reliably with an accuracy of 98–99%. Its reported sensitivity for the detection of breast cancer ranges from 58% to 72% and there is some overlap of features between benign and malignant masses. The aims of this study are: (1) to study the effects of breast ultrasound on patient management at the stage of assessment, and (2) to identify the types of mammographic and clinical abnormality where breast ultrasound is of value. Breast ultrasound was performed on 287 of 296 women recalled for assessment out of the first 3559 screened in the Camberwell Breast Cancer Screening Service. The women were first assessed by further mammography. The type of abnormality was recorded and a recommendation for further management made (RR = routine recall, ER = early recall, BX = Biopsy). Following ultrasound examination, the abnormality was again classified (normal, cyst, solid benign, solid malignant, solid indeterminate) and a recommendation for further management made. The results of any biopsies performed were recorded. The impact of ultrasound examination on management at the time of assessment is discussed with reference to the type of mammographic abnormality being assessed and in the context of the acceptable cancer detection rates and benign-to-malignant biopsy ratios suggested in the Pritchard Report on Quality Assurance in Mammography Screening.

Ultrasound diagnosis of bilateral varicocoele and its clinical significance

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Scrotal ultrasonography has been used as a diagnostic method for testicular pathologies because of its versatility and clear resolution of surrounding structures within the scrotum. The diagnosis of varicocoele in the past was based primarily on physical palpation and confirmed by sophisticated, traumatic and sometimes very dangerous invasive methods which are now out of use. The evidence gathered so far demonstrates that varicocoeles are detrimental to spermatogenesis and this effect is unrelated to their size or location (unilateral or bilateral). Thus, physicians should be able to have other diagnostic methods other than physical examination to detect and/or confirm the presence of even the small but clinically important bilateral varicocoele. Fifty men so far have been included in this study. Scanning was carried out with a real time linear scanner using a 5 MHz transducer. The radiologist was blind to the clinical and laboratory findings of the patient. Our preliminary results show a marked incidence of bilateral varicocoeles in patients that have abnormal semen analysis as compared with patients with normal semen analysis. There was also a higher detection of bilateral varicocoele by ultrasonography than by physical examination. These results enable us to conclude that ultrasonography is a reliable and non-invasive method in the diagnosis of small subclinical bilateral varicocoeles.

The use of real-time ultrasound in the management of scrotal trauma

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Scrotal trauma often gives rise to difficulties in clinical assessment because of pain, tenderness and swelling. Using real-time high frequency (7.5 MHz) ultrasound, high quality images of the scrotal contents can always be obtained. The nature of the injury can thus be clearly defined with minimal patient discomfort. We present the findings from ultrasound scans in 26 patients following scrotal trauma, seen at King's College Hospital from 1984 to 1989 (age range 5–68 years). Twenty-two of the patients showed an ultrasound abnormality and in five of these there were signs of testicular damage. The ultrasound appearances of the different types of scrotal injury are demonstrated and their implications for management are discussed.

Transrectal ultrasound in the investigation of haemospermia

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AIM: to review the trans-rectal ultrasound findings in a series of patients with haemospermia and to assess the role of ultrasound in the investigation of this condition. METHOD: fifty-two patients presenting with haemospermia underwent transrectal ultrasonography using a 4 MHz hand-held radial transducer. FINDINGS: nine patients had normal scans. There was evidence of benign prostatic hypertrophy in 24 patients; in most patients this was of mild degree. Seminal vesicle abnormalities were noted in 10 patients. Calcification within the prostate was noted in 32 patients: in eight it was central and in 21 it was more peripheral within the prostatic ducts. In five of these cases the calcification was florid and bilateral. No cancers were detected. DISCUSSION: the relative frequency of underlying disease in reported series of patients with haemospermia depends upon the degree of investigation undertaken; in some studies tests have been invasive. Transrectal ultrasound provides a simple, relatively non-invasive method to assess the prostate and seminal vesicles. We found scan abnormalities in 43/52 (83%) of cases or 39/52 (75%) cases if BPH is excluded. Ultrasonography is able to demonstrate many abnormalities associated with haemospermia including prostatitis, duct calcification and seminal vesicle abnormalities, and can exclude an underlying prostatic neoplasm. It is recommended as the initial, and possibly the only, imaging investigation in patients presenting with haemospermia.

Sonographic detection of foreign bodies of the extremities

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Conventionally, radiography is used for the detection of foreign bodies in the extremities and fluoroscopic screening for localization during surgery. A prospective study to evaluate the accuracy of ultrasound in the detection and localization of foreign bodies was undertaken. Forty-five cases were chosen, of which 20 cases had radiographically proven radio-opaque foreign bodies of different sizes. In 25 cases, there were clinical suspicions of foreign bodies with minimal or no radiographic indication of foreign bodies. Examinations were carried out with TOSHIBA SAL 77A and SIEMENS SL2 and 5 MHz and 7.5 MHz probes were used. A positive sonographic identification of foreign body was made when a well-defined echo-reflective shadow was noted in the soft tissue with distal acoustic shadowing. Occasionally echo-poor areas were noted surrounding foreign bodies, suggesting oedema or small abscess formation. In three cases, sonographic localization of deep-seated radio-opaque foreign bodies was also carried out. The site of incision and the depth of the foreign body from the skin surface were indicated. Of 20 radiographically proven cases of foreign bodies, 19 were detected on sonographic examination. Failure of the solitary case was thought to be due to small size of the foreign body and presence of gas in the soft tissue, noted on the radiograph. Among 25 cases of suspected foreign bodies 7 cases had positive sonographic detection. At surgery, foreign bodies were found in five cases; in one case horny calcific material was removed and in one case exploration was negative. Among five positive explorations three cases had glass particles and two cases had wooden splinters. Ultrasonic localization of all three cases was proved to be accurate. Sonography can therefore be gainfully employed in the detection of faintly radio-opaque or radiolucent foreign bodies in the extremities and deep seated foreign bodies can be localized without the need for fluoroscopic screening.

Veterinary ultrasound

Chairmen: D. P. Attenburrow and S. Richardson

Equine echocardiography, by M. W. Patteson
Ultrasound investigation of the uterus and ovaries of the mare, by W. Allen
The use of ultrasound scanning to breed leaner lambs, by G. Simm
Predicting the time of ovulation in the bitch, by J. S. Boyd, J. M. Ferguson, M. J. Harvey and J. P. Renton
Ultrasonographic events during pregnancy in the bitch, by G. C. W. England and W. E. Allen
Experiences with equine abdominal ultrasonography, by M. H. Hillyer
Ultrasound examination of pregnant bottlenose dolphins, by R. S. Wyburn, P. Williamson and N. J. Gales

Equine echocardiography

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Ultrasound machines capable of making high quality images of horse's hearts are now available at a cost which is within the reach of practising veterinary surgeons. In order to make use of this valuable diagnostic aid, knowledge of the appropriate techniques, normal echocardiographic anatomy and the appearance of pathological changes must be acquired. In this paper, the transducer positions used to produce standard echocardiographic images are described and normal anatomical features are demonstrated, with emphasis on areas of potential confusion and the appearance of artefacts. Recent work on anatomical validation and left ventricular volume determinations are summarized. The indications for echocardiographic examination are discussed and some pathological conditions are illustrated.

Ultrasound investigation of the uterus and ovaries of the mare

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The fate of 300 mature oestrous follicles was followed by daily ultrasound examination in a group of 51 mares which included ponies and thoroughbreds. Normal ovulation was detected on 264 (88%) of occasions. Lutenization of follicles, without rupture, occurred in both ovaries (19 in the left, 17 in the right) and was diagnosed when a follicle retained its shape and size but became cloudy to varying degrees owing to haemorrhage from the follicle wall. No seasonal effect on this phenomenon was seen, but some mares appeared more prone to ovulation failure than others. Luteal activity, as judged by jugular plasma progesterone concentrations, was similar after normal ovulation and lutenization without follicle rupture. However, in many cases progesterone concentrations began to rise before gross ultrasonographic signs of lutenization were seen in follicles which did not ovulate. The presence of intraluminal uterine fluid was monitored in 250 mares visiting a commercial stud. Accumulations of clear fluid in early oestrus were associated with endometrial oedema and occurred in mares with cervical stenosis. This suggests that all mares produce uterine fluid in oestrus, but that it normally drains spontaneously. All mares were examined after mating and ovulation, and gross accumulations of fluid were removed before antibiotic therapy. It is suggested that endometritis can be recognized by ultrasonography and resolved in many cases by this treatment regime.

The use of ultrasound scanning to breed leaner lamb

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Over the past 40 years lamb consumption in Britain has declined from around 11 kg per head per year to around 6.5 kg. One of the major reasons for this is overfatness. The fatness of all animals is influenced by a number of environmental and genetic factors, including age, live weight, food quantity and quality, sex, breed and genotype within breed. Although manipulation of each of these factors can play an important role in reducing fatness, genetic improvement is particularly important because it is permanent, cumulative and usually highly cost-beneficial. Ultrasonic measurements of fat and muscle depth in the loin region can be useful in *in vivo* estimation of carcass composition. A selection index, or scoring system, has been derived at the Edinburgh School of Agriculture (ESA) to incorporate such measurements from a real-time 'B'-mode scanner, together with live weight, into a single score to identify superior animals for breeding. After 4 years of selection on this index in an experimental flock, selection line ram lambs are showing advantages of +2.6% live-weight, +6.2% muscle depth, −7% fat depth and +7.8% in overall index score, compared with unselected control lambs. The scanning technique and the index developed at the ESA are now in widespread use in the UK sheep industry, via the Meat and Livestock Commission's Sheepbreeder recording scheme.

Predicting the time of ovulation in the bitch

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Identification of the precise time of ovulation in the bitch remains a controversial process. Methods used are observation of behaviour during the oestrous period, assay of circulating progesterone levels and ultrasonography. The purpose of this project was to assess the correlation of the times of prediction of ovulation obtained by the above methods and comparing the results with the estimation of age of harvested ova. Ten bitches were followed from the first day of oestral bleeding until ova were harvested at 4–6 days after the time when ovulation was estimated to have occurred. The bitches were scanned using a 7.5 MHz sector transducer applied bilaterally in the mid flank region, but the ovaries were difficult to image consistently during the early phase of the oestrous period. At the time of ovulation there was a dramatic alteration in ovarian size and in the echogenicity of the contained structures, allowing more ready demonstration of the organs. The use of ultrasound scanning as a comparator to detect ovulation are discussed.

Ultrasonographic events during pregnancy in the bitch

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Data on the early diagnosis of canine pregnancy and of foetal development using ultrasound are confused because many workers have assumed that pregnancy begins on the first day of mating. This may produce apparent pregnancy lengths of between 54 and 72 days. In the present study foetuses were aged retrospectively in relationship to the calculated surge of luteinizing hormone (LH), which occurs 65 days before parturition. Six bitches of mixed breeding were imaged daily for 40 days after mating using 7.5 MHz linear and sector transducers. The earliest time a gestational sac could be imaged was 21 days after the calculated LH surge. Sixty-six bitches (labrador retrievers, golden retrievers and labrador × golden retrievers) were then examined as frequently as possible commencing 28 days after mating; of these 50 whelped. On the first examination only one bitch was wrongly diagnosed as being non-pregnant (24 days after the calculated LH surge). Foetal growth was monitored and the times at which various organ systems could be imaged were recorded. Regression coefficients were calculated for size of conceptus, occipito-sacral length, thoracic width and biparietal diameter; these were found to be significantly related to gestational age ($p < 0.001$). One case of confirmed pregnancy followed by resorption was monitored in a separate bitch.

Experiences with equine abdominal ultrasonography

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Ultrasonography is a routine technique for the diagnosis and evaluation of abdominal disease in man and small animals. In the horse the widespread use of abdominal ultrasonography has been limited to examination of the female reproductive tract. However, more recently there have been reports of its use in evaluating other abdominal organs. This paper will describe the practical uses and limitations of ultrasonography in the diagnosis of equine abdominal disease. Routine clinical examinations for the investigation of certain abdominal organs will be described together with their normal ultrasonographic appearance. Selected cases of abdominal disease in the horse, where ultrasonography was an important part of the clinical diagnosis, are also presented.

Ultrasound examination of pregnant bottlenose dolphins (*Tursiops truncatus*)

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In 1981, four female and three male juvenile bottlenose dolphins (*Tursiops truncatus*) were captured in the Indian Ocean and held in a marine park located close to Perth, Western Australia. As part of the husbandry routine they were weighed monthly. In June 1988 a marked weight gain was recorded in two of the female dolphins and it was suspected that they were pregnant. Ultrasound examination was therefore carried out on the four females. All were found to be pregnant. As no data could be found which would allow the stage of pregnancy to be determined it was decided to carry out regular ultrasound examinations until parturition in order to monitor foetal growth to provide a future base which could be used to establish foetal age. The dolphins were trained to come to the side of the pool and turn upside down, presenting their ventral abdomens. The ultrasound examination was carried out with a 3.5 MHz linear array transducer. A detailed study was difficult as the dolphins would only remain in position for 15–30 s. The best position for the probe was found to be across the abdomen 2/3 of the distance between the genital slit and the umbilicus. In later pregnancy the best images of the foetus were obtained with the probe held parallel to the long axis of the body and between 10 and 20 cms to the left of midline. The earliest that a clear image of the pregnant uterus could be seen was 35 weeks prior to parturition. As pregnancy is reported to last for 50 to 52 weeks, this would be at 15 to 17 weeks of gestation. Of the measurements taken it was found that the most reliable estimates of foetal age were obtained from the transverse diameter of the thorax at the level of the heart and the skull diameter (occipital-frontal axis).

Abdominal ultrasound

Chairmen: H. Meire and N. Ring

The accuracy of ultrasonography compared with intravenous urography in investigating haematuria, by D. Lindsell, R. Mastorakou and J. Spencer

Ultrasound compared with intravenous urography in the investigation of adult urinary tract infection: a prospective study, by R. Mastorakou, J. Spencer and D. Lindsell

Echogenic rings around the pyramids—the appearances of early nephrocalcinosis, by B. Al-Murrani, M. Blaszcyk, D. O. Cosgrove and W. E. Svensson

The role of emergency ultrasonography in the management of the acute abdomen, by E. Carmody, F. P. McGrath and F. Keeling

A prospective study of the role of ultrasound in the investigation of patients with a right iliac fossa mass, by F. C. Millard, M. C. Collins and R. J. Peck

Total hepatic blood flow—can Doppler do it? by K. M. Carlisle, M. Halliwell, A. E. Read and P. N. T. Wells

Doppler ultrasound in the investigation of hepatic parenchymal disease, by J. I. S. Rees, A. Whyte and D. L. Cochlin

Small bowel thickening—A new ultrasound sign in portal hypertension, by D. Macvicar, S. Saverymuttu, A. Grammatopoulos and A. E. A. Joseph

Hepatic sonography in AIDS, by P. C. Rowlands, M. McCarty, and M. E. Crofton

Another cause of thickwalled gallbladder: malignant lymphatic obstruction, by C. Metreweli and I. Stewart

The accuracy of ultrasonography compared with intravenous urography in investigating haematuria

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It has been standard urological practice to request an intravenous urogram (IVU) as the primary imaging study in the investigation of adults with haematuria. The role and value of ultrasound (US) has not been established. A prospective comparative trial of the value of US *versus* IVU in adults with haematuria is described. Ninety patients (67 male and 23 female) referred for IVU by general practitioners and the outpatient departments were examined concurrently with both investigations. The US study was performed during the IVU but the bladder was not formally filled for the study. They were reported independently and the eventual diagnosis established after seeking additional clinical and radiological data. In 42 patients (46.7%) both investigations were normal. Of the abnormal studies, after prostatic enlargement, the commonest findings were bladder tumours (22.9%) and urinary calculi (18.8%). Overall, ultrasound agreed with the findings of urography in 96.7% of cases with no significant abnormalities missed. One small calculus was missed in a kidney containing larger calculi. No urothelial tumours of the upper tracts were encountered. Ultrasound detected three early bladder tumours with sizes ranging from 5 to 20 mm not visible on urography, 21.4% of those found in the series. It was able to clarify the nature of the renal "masses" evident on five urograms (simple cysts). Ultrasound provides a safe and accurate method of imaging the urinary tract in adults with haematuria and should replace urography as the initial imaging investigation supplemented by a plain abdominal radiograph where urinary calculi are likely. If clinical suspicion is of urothelialneoplasia an IVU is advisable. In addition to the reduced hazards to patients from ionizing radiation and intravenous contrast media, significant savings in cost and time per patient examined would result.

Ultrasound compared with intravenous urography in the investigation of adult urinary tract infection: a prospective study

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The investigation of adults with urinary tract infection (UTI) continues to produce a sizeable demand for intravenous urography (IVU). Whereas ultrasound (US) has replaced IVU in the examination of children with UTI, its role and efficacy in investigating adults is not clearly established. A prospective comparative trial of the value of US *versus* IVU in adults with proven UTI is described. Ninety-four consecutive patients (52 female and 42 male) referred from either general practitioners or the out-patients departments for IVU were examined concurrently with both investigations. The US studies were performed during the IVU study but the bladder was not formally filled for the purposes of the US examination. They were reported independently. In 69 patients (73.4%) both investigations were normal. Overall, ultrasound concurred with the findings of urography in 93.6% of cases, and when a single abdominal radiograph was added this increased to 95.7%. The commonest abnormality, prostatic enlargement, had been suggested from clinical features as the likely diagnosis. The degree of enlargement was better shown by US. Ultrasound missed only one important diagnosis, mild papillary necrosis in normal sized non-scarred kidneys. (Two minor anatomical variants and a small bladder diverticulum were missed by US.) It detected one early bladder tumour not visible on urography and clarified the nature of renal "masses" evident on three urograms (simple cysts). The investigation of adults with UTI has a low yield of significant abnormal findings, particularly in women. Ultrasound provides a safe and accurate method of imaging the urinary tract and should replace urography as the initial imaging investigation. Considerable reductions in cost and time per patient examined and in patient morbidity will result.

Echogenic rings around the pyramids—the appearances of early nephrocalcinosis

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Echogenic lines at the corticomedullary junctions of the kidneys were incidental findings in six patients on abdominal ultrasound scans; they form striking petal-shaped rings that outline the peripheries of the renal pyramids. Four of our patients had carcinoma of the breast, one lymphoma and one had a seminoma of the testis. Four were female and two male, with an age range of 25–50 years. The intense echoes suggest calcification, but the pattern is not the classical reversal of the corticomedullary ratio of nephrocalcinosis. However, if these studies had been performed early in the course of the calcification, or if the hypercalcaemia responsible had been corrected previously, the process would have been imaged at an early or arrested stage. Correlation with CT scans in two patients demonstrated curvilinear bands of high density in the same position, confirming the interpretation that the appearance is due to calcification. In one case where an autopsy examination of the kidneys was performed, early calcification was found at the corticomedullary junctions. On abdominal X-rays no renal calcification was seen in two patients while one showed calcification in the renal parenchyma, confirming observations by others that ultrasound is more sensitive than plain radiology in nephrocalcinosis. Based on these observations, we propose that nephrocalcinosis at its earliest detectable stage produces curvilinear echogenic bands at the corticomedullary junctions, with subsequent progression to the more familiar form of echogenic pyramids if the hypercalcaemia persists.

The role of emergency ultrasonography in the management of the acute abdomen

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A 24 h emergency ultrasound facility was offered to the clinicians for patients presenting with acute abdominal pain of less than 24 h duration. Only those patients who had been assessed by an experienced clinician and were due for admission were accepted for this study. When the clinicians had reviewed the results of the emergency investigations requested, *e.g.* plain radiology, biochemistry, haematology etc., they were asked to list three differential diagnoses in descending order of likelihood. This information was withheld from the radiologist. Real time upper abdominal ultrasound was then performed in a systematic fashion (a pelvic examination was included where indicated) using 3.5 MHz/5 MHz sector probes. Seventy-five patients were included in the study. The admitting clinician was given the result of the ultrasound scan. When the patient was discharged the ultrasound findings were classified under five separate headings: (a) ultrasound uniquely diagnostic, *i.e.* diagnosis not listed in the differential diagnosis, (b) ultrasound confirmed the suspected primary diagnosis, (c) ultrasound confirmed the second or third listed differential diagnosis, (d) ultrasound was non-diagnostic and of no value in the patient's further management, (e) ultrasound was misleading. There were 14 patients (18.7%) in group A, 26 patients (34.7%) in group B, nine patients (12%) in group C, 24 patients (32%) in group D and two patients (2.6%) in group E. Ultrasound confirmed the suspected primary clinical diagnosis in 34.7% of patients and enabled us to disregard the primary diagnosis in 12% of patients in favour of a second and third differential diagnosis. Most significantly it confirmed a completely unsuspected diagnosis in 18.7% of patients. Therefore 30.7% of patients (group A, group C) had their management directly altered by the availability of ultrasound. Of the 14 patients (18.7%) who had a completely unsuspected diagnosis made on ultrasound, 12 were female within the reproductive age group with gynaecological pathology. Emergency ultrasound has proved most useful in young female patients presenting with acute abdominal pain.

A prospective study of the role of ultrasound in the investigation of patients with a right iliac fossa mass

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Patients presenting with a right iliac fossa (RIF) mass are a constant diagnostic problem. The objective of this study was to assess the role of ultrasound (US) in their investigation. A prospective series of 50 patients presenting with a clinically suspected RIF mass was examined by US, and the findings correlated with further imaging and/or final clinical outcome. In 80% there was a positive finding on the US examination. Within the gastro-intestinal tract the findings included caecal carcinoma, appendix mass and thick-walled bowel proving to be Crohn's disease, and lymphoma. In many cases, however, the pathology arose from outside the gastro-intestinal tract. From the genito-urinary tract, findings included hypernephroma, polycystic kidneys, ovarian cysts, ovarian carcinoma and ectopic pregnancy. The gastro-intestinal and genito-urinary tracts provided the majority of pathology, but other findings included lymphadenopathy and aortic aneurysm. In some cases the findings were due to normal variants of anatomy such as Riedel's lobe and low-lying kidney. In several cases no abnormality was found, and despite further imaging or clinical follow-up there have been no false negatives. There has been one false positive study suggesting bowel wall thickening, not confirmed at barium study. In conclusion, US is recommended as the imaging modality of first choice in patients presenting with an RIF mass. It can reliably assess the organ of origin and probable nature, and can also direct further imaging techniques as may be necessary.

Total hepatic blood flow—can Doppler do it?

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The total blood flow into the liver is of considerable academic interest and is probably of clinical importance in the management of hepatic disorders. The liver has two main sources of blood: the portal vein and the proper hepatic artery. Volume flow in the portal vein has been measured by several groups using duplex ultrasound. Only one report describes arterial flow quantification and this is in the common hepatic artery, a vessel which carries both hepatic and gastric blood supply. Measurements in the proper hepatic artery have not been reported. A group of 40 normal individuals was scanned with a view to determining a sub-set in whom appropriate visualization of both the common and proper hepatic arteries was possible. From this sub-set (about 30% of the total group), values for the volume flow in both vessels have been determined. We plan to test whether, in the fasting state, the ratio of common-to-proper hepatic flows is constant. The significance of these results for the investigation of total hepatic haemodynamics are discussed, especially in view of the limited applicability of hepatic artery measurements in the normal population.

Vessel	Mean velocity (cm/s)	Mean volume flow (mc/min)	Total population *n* = 30
Common hepatic	15.45 ± 1.87	262.1 ± 170 ml/min	(*n* = 19)
Proper hepatic	24.35 ± 1.51	183.2 ± 76 ml/min	(*n* = 10)
Portal vein	13.85 ± 2.59	796.2 ± 148.9 ml/min	(*n* = 27)

Doppler ultrasound in the investigation of hepatic parenchymal disease

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Hepatic parenchymal disease may modify flow in the hepatic veins, changing the flow from the normal "ACV swing" pattern to continuous hepatofugal flow. The flow in the portal veins may also be modified as a response to portal hypertension and the formation of varices. We studied 20 patients with hepatic parenchymal disease, the type of disease being unknown to the operator, but fully documented from previous history, test and biopsy. Twenty control patients were also studied. Subsequently, the pattern of Doppler change was correlated with the clinical diagnosis. We found that the greatest change in hepatic venous flow occurred in alcoholic cirrhosis, while in cirrhosis secondary to hepatitis, these changes were less marked. Haemochromatosis and steatosis showed no change. Splenorenal varices were found in a number of cases, some of whom have no evidence of oesophageal varices. We conclude that hepatic Doppler studies are a valuable adjunct to the study of liver sonodensity in hepatic parenchymal disease, having particularly characteristic changes in acoholic cirrhosis. They may also detect unsuspected varices.

Small bowel thickening — a new ultrasound sign in portal hypertension

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Abdominal ultrasound in patients with portal hypertension may reveal a variety of extra-hepatic signs, such as splenomegaly and varices. Thickening of the gall bladder wall is a recognized finding in cirrhosis, and more recently "congestive gastropathy" has been recognized as a thickening of the stomach wall in portal hypertension. We report a series of 13 patients with portal hypertension in whom the thickness of gall bladder wall and/or stomach wall was found to be increased. In 11 of these 13 patients the small bowel wall was also thickened, producing a "target" appearance. This ultrasound sign has not previously been described in portal hypertension. Jejunal widening and thickening of mucosal folds have been described on barium small bowel studies in cirrhosis and this has been attributed to hypoalbuminaemia. However, hypoalbuminaemia was not associated with small bowel thickening seen on ultrasound in all our patients. It seems likely that a situation analogous to congestive gastropathy, with dilated tortuous submucosal blood vessels, exists in the small bowel. The appearances of small bowel thickening in portal hypertension will be illustrated. Data correlating thickening of small bowel, stomach and gall bladder wall will be presented. It is important to recognize this finding in portal hypertension so that it would not be attributed to intrinsic bowel disease.

Hepatic sonography in AIDS

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Ninety-five ultrasound examinations of the liver and upper abdomen were carried out in patients with AIDS and HIV seropositivity, of which 20% were abnormal. Several patterns of abnormality were observed. These were: diffuse decrease in echogenicity; diffuse inhomogeneity; diffuse increase in echogenicity; biliary duct dilatation and irregularity; focal lesions. Plasma biochemistry and serology results were reviewed and biopsy was performed in most of the patients with abnormal sonographic findings. CT was carried out in many of the patients. Diffuse hypoechogenicity was usually due to coexisting viral hepatitis. Diffuse inhomogeneity and increased echogenicity were caused by fat infiltration and also by Kapsoi's sarcoma as well as lymphoma. Focal lesions were due to tuberculosis, lymphoma, metastases and Kapsoi's sarcoma. Biopsy was usually required to differentiate these conditions before treatment. Biliary abnormality was usually due to cryptosporidiosis.

Another cause of thickwalled gallbladder: malignant lymphatic obstruction

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Many causes of thickening of the gallbladder wall have been described, including bacterial and viral inflammation, malignant infiltration, hypoalbuminaemia and adenomyosis. We have seen four cases in whom an oedematous gallbladder was found but there did not appear to be any previously described cause. All these patients had portal hilar lymphadenopathy in addition to other signs of malignancy. Not all cases of portal hilar lymphadenopathy are accompanied by gallbladder oedema, but when the critical junction of lymphatic drainage is affected even by subtle lymphadenopathy then lymphoedema will supervene. Awareness of this occurrence will guide the echographer to disease in the portal hilar region in diagnostic dilemas and more accurate diagnosis.

Obstetric ultrasound

Chairmen: S. Wood and J. Foulkes

Is karyotyping for choroid plexus cysts necessary? by J. G. Thorpe-Beeston, C. M. Gosden and K. H. Nicolaides
Choroid plexus cysts— a marker for Trisomy 18. A prospective study and review of the literature, by P. Twining, J. Zuccollo, J. Swallow and J. Clewes
The diagnosis of anterior abdominal wall defects—how good is "routine" ultrasound? by S. A. Walkinshaw, G. Hebish and E. Hey
Safety of fetal blood sampling from the intrahepatic vein, by P. K. Nicolaidis, V. Nicolini, N. M. Fisk, Y. Tannirandorn, C. E. Ellis and C. H. Rodeck
Ultrasound diagnosis of the growth retarded and growth discordant twin fetus, by M. J. Rasmussen, R. Connolly, M. J. Turner and J. S. Strong
A new biophysical variable: observation of fetal mouthing, by M. Pillai and D. James
Adrenal scanning in intrauterine growth retardation, by S. Swinney, C. Hayden, D. Freathy, A. Phillips, C. Orme, P. Smith and H. Ruddick
Middle and cerebral artery flow velocity waveforms obtained by colour flow imaging in appropriate and small for gestational age fetuses, by S. Vyas, K. H. Nicolaides, S. Bower and S. Campbell
Transvaginal ultrasound in the serial assessment of the cervix in twin pregnancies, by A. P. Smith, B. H. Lim and N. C. Smith
Placental localization using transvaginal ultrasound, by A. P. Smith, B. H. Lim and N. C. Smith

Is karyotyping for choroid plexus cysts necessary?

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Chromosomal defects were detected in 13 out of 30 (43%) fetuses with choroid plexus cysts where karyotyping was performed in samples obtained by cordocentesis. All chromosomally abnormal fetuses (Trisomy 18, $n = 10$; Trisomy 13, $n = 1$; Translocation, $n = 2$) had additional malformations including exomphalos ($n = 3$), oesophageal atresia ($n = 2$), congenital diaphragmatic hernia ($n = 3$), congenital heart disease ($n = 2$), facial cleft ($n = 2$) and hydrops ($n = 1$). Furthermore, 11 of the fetuses were small for gestational age and had subtle malformations including abnormalities of the hands and feet ($n = 10$) and diamond shaped heads ($n = 4$). In the group of 17 chromosomally normal fetuses the choroid plexus cysts were either isolated ($n = 8$) or associated with renal malformations ($n = 6$), exomphalos ($n = 1$) or congenital heart disease ($n = 2$).

Choroid plexus cysts—a marker for Trisomy 18. A prospective study and review of the literature

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In order to determine the incidence and significance of choroid plexus cysts a prospective study was carried out on all fetuses scanned at Queen's Medical Centre, Nottingham. Over an 11 month period 4541 singleton pregnancies were scanned at 18–19 weeks gestation and 19 fetuses were identified with choroid plexus cysts. The incidence of cysts is 0.42%. (The incidence in other series ranges from 0.18 to 0.8.) Cysts were unilateral in 10 cases and bilateral in nine cases. The size of the cysts varied from 3 to 12 mm in diameter with an average diameter of 6.2 mm. Choroid plexus cysts were associated with other abnormalities in three cases. In one case a diaphragmatic hernia with bilateral radial aplasia was demonstrated. The fetus was terminated and chromosomal studies revealed a Trisomy 18. A second fetus had a small omphalocoele; amniocentesis showed a normal karyotype. A third fetus initially scanned at 18 weeks subsequently developed duodenal atresia at 22 weeks and other ultrasound markers for Downes syndrome were also demonstrated. The patient declined amniocentesis and the pregnancy is ongoing. All choroid plexus cysts seen at 18 weeks had resolved or were decreasing in size when patients were rescanned at 22 weeks. A review of the literature including our own series reveals 172 cases of choroid plexus cysts previously reported. There have been 11 cases of Trisomy 18 and one case of Trisomy 21 associated, this gives an incidence of 6.4% for Trisomy 18 in fetuses with choroid plexus cysts. In addition, a recent study of 14 cases of Trisomy 18 showed choroid plexus cysts in 70% of fetuses under 26 weeks gestation. We therefore feel that choroid plexus cysts are a useful marker for Trisomy 18 and the ultrasound markers for Trisomy should be sought whenever choroid plexus cysts are seen. The ultrasound markers for Trisomy 18 and the ultrasound markers for Trisomy should be sought whenever choroid plexus cysts are seen. The ultrasound markers for Trisomy 18 will be demonstrated both ultrasonically and from pathological specimens. To conclude, in patients with choroid plexus cysts detected at 18–20 weeks, a careful detailed scan should be carried out to look for the ultrasound markers of Trisomy 18. If there is an associated abnormality a karyotyping should be carried out. The incidence of Trisomy 18 in fetuses with choroid plexus cysts is 6.4%.

The diagnosis of anterior abdominal wall defects—how good is "routine" ultrasound?

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The Northern Regional Fetal Abnormality Survey collects data on both prenatally suspected fetal anomalies and on confirmed abnormalities postnatally whether suspected or unsuspected. The survey therefore allows audit of the ability of antenatal ultrasound to detect and describe accurately specific groups of abnormalities within a geographically defined population which includes both district and referral units. As prenatal diagnosis and obstetric management of the two different types of anterior wall defects differ markedly, accurate diagnosis is an integral part of the management. Between 1984 and 1988, 115 suspected or confirmed anterior abdominal wall defects were reported to the survey. Seventy-nine abnormalities (gastroschisis, exomphalos, and complex syndromes which include anterior wall defects) were suspected prenatally, of which four (5%) were false positive diagnoses. Two of these had other lethal anomalies, but two were normal, one undergoing amniocentesis and resulting in a neonatal death following spontaneous premature delivery at 24 weeks. Excluding complex syndromes, 81 of the 93 confirmed cases of exomphalos or gastroschisis had an ultrasound examination between 16 and 24 weeks, with anterior wall defects being correctly identified in 48 (59%) of these. Fifty-two defects were suspected on initial planned examination, of which 38 were referred for assessment centrally. In six cases of exomphalos the diagnosis was correctly revised; to gastroschisis in four, a complex syndrome in one and to normal in one. The prenatal diagnosis of gastroschisis was confirmed at delivery in 15 of 16 defects. The diagnosis of exomphalos was confirmed at delivery in 27 of 34 cases, five being gastroschisis (one undergoing therapeutic termination), one a complex syndrome and one normal. The overall rate of misdiagnosis was 16%. The survey has demonstrated what is currently achieved by "routine" diagnostic ultrasound in prenatal diagnosis within a defined population. Continuing review of the survey will be useful in monitoring improvements in diagnostic ability.

Safety of fetal blood sampling from the intrahepatic vein

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Access to the placental cord insertion is difficult in the presence of abnormalities of amniotic fluid volume, maternal obesity, or when the fetus obscures a posterior placental cord insertion. In these situations, FBS can be performed at the intrahepatic vein (IHV). One hundred and sixty eight IHVFBS procedures were performed in 134 patients (138 fetuses) between 15 and 36 weeks, including 64 transfusions. Indications were: Rh alloimmunization in 64, rapid karyotyping 60, IUGR 18, prenatal diagnosis 23, and thrombocytopenia in three. One hundred and forty one (83.9%) were primary attempts at the IHV, while 27 (16%) followed a failed attempt at the cord insertion. There were 14 (8.3%) failures at IHVFBS; fetal blood was successfully obtained from another site in nine, one fetus underwent an intraperitoneal rather than an intravascular transfusion, and FBS was abandoned or postponed in five. Immediate complications comprised intraperitoneal bleeding in four and bradycardia in two, but all fetuses recovered. Overall there were 37 perinatal losses amongst continuing pregnancies and all but one of these were in pregnancies with other risk factors such as severe IUGR, major malformations, or multiple transfusions. No loss was specifically attributable to IHVFBS. To assess any hepatocellular damage from IHVFBS, liver function tests were assayed in 32 non-hydropic Rh fetuses undergoing serial intravascular transfusion. Pretransfusion alkaline phosphatase, alanine and aspartate aminotransferases, and gamma glutamyl transpeptidase (GGT) were similar in 13 fetuses undergoing IHVFBS/transfusion (Group I) and 13 undergoing FBS/transfusion at the cord insertion (Group II). There was a significantly greater short-term change, albeit small, in GGT (post-pretransfusion levels) in Group I (median 3IU/l, range −7 to +49) compared with Group II (median −1, range −7 to +7, $p = 0.02$). No other significant differences were observed for any of the enzymes in short-term or long-term changes. In conclusion, IHVFBS appears to be both a safe and a practicable alternative to "cordocentesis". We advocate a flexible approach to FBS, with the site of sampling chosen at the time of the procedure.

Ultrasound diagnosis of the growth retarded and growth discordant twin fetus

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Prematurity remains the major perinatal hazard facing twin pregnancy. Such pregnancies also face a high risk of intrauterine growth retardation and discordant fetal growth, with an associated increase in perinatal morbidity and mortality. Antenatal ultrasound assessment offers the potential for early confirmation of twin pregnancy, the recognition of major fetal malformation, the assessment of zygosity, the assessment of fetal well being, and also for the diagnosis of intrauterine growth retardation, allowing an increased fetal surveillance, and appropriate timing and mode of delivery. The aim of this study was to analyse our ability to predict by antenatal ultrasound assessment the growth retarded and growth discordant twin. Retrospective analysis was performed on results obtained from 102 consecutive sets of surviving twins attending the hospital twin clinic for antenatal ultrasound assessment. Estimated fetal weight was calculated using the biparietal diameter if feasible and abdominal circumference, with the most recent predicted fetal weight and estimated discordancy compared with results at delivery. Standard hospital centile charts of weight for gestation were used. The mean number of ultrasound assessments was 3.2 and the mean interval between weight estimation and delivery was 12 days. Of the 204 twins delivered, 65 infants (31.9%) of 44 pregnancies (43.1%) were below the tenth centile of weight for gestation, with 53 infants (30.0%) of 38 pregnancies (37.3%) also below the fifth centile. Growth discordancy of greater than 25% was observed in 11 pregnancies (10.8%). Ultrasound identification of growth retardation ($\leqslant$ 10ile) had a sensitivity of 0.52 and a specificity of 0.86, with results for the detection of infants under the fifth centile no better. Identification of growth discordancy ($\geqslant$ 25%) had a sensitivity of only 0.18 and a specificity of 0.96. Ultrasound assessment of fetal weight in twin pregnancy is technically difficult, and even when including measurements of the abdominal circumference up to half of all growth retarded twins may be missed. Intrauterine growth retardation is common in twin pregnancy; antenatal management must allow for this fact while improved methods of detecting the growth retarded twin are sought.

A new biophysical variable: observation of fetal mouthing

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In late pregnancy human fetuses exhibit well-developed behavioural states (called 1F and 2F), which closely resemble quiet sleep and rapid eye movement sleep after birth. About one third of the time is spent in state 1F, which is characterized by absence of eye movements and somatic movements and an unreactive fetal heart rate pattern. Episodic fetal breathing may occur, but significantly less often than during state 2F ($p < 0.001$). The most common type of fetal movement observed during state 1F is bursts of rhythmical mouthing. Intervals of this behavioural state usually last 20–30 min, and not longer than 40 min. In a group of 80 healthy fetuses we found that the average time to achieve a satisfactory biophysical score and non-stress test in association with state 1F was 26.3 min and 27.0 min respectively, and 44.0% and 52.6% respectively failed to achieve a "normal" result. In contrast, satisfactory results were always obtained during intervals of state 2F, within an average of 3–5 min. We attempted to observe fetal mouthing during biophysical assessment on 69 mature fetuses, 29 of whom were considered high risk. In four of the 29 high risk fetuses normal behavioural states could not be identified in recordings lasting longer than 40 min, and fetal mouthing movements were absent in all four. Objective evidence of fetal compromise (of different aetiologies) to account for these findings was present in all four. In the remaining 65 fetuses normal behavioural states were identified, and rhythmical mouthing identifiable during state 1F significantly more often than the variables scored for in the non-stress test and biophysical profile, with the exception of liquor volume (the only state-independent variable). Because most biophysical variables are state dependent, evaluation in the light of knowledge of normal patterns of fetal behaviour is likely to be superior to any arbitrarily defined scoring system.

Adrenal scanning in intrauterine growth retardation

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The diagnosis of intrauterine growth retardation remains a challenge to obstetric management. Clinical methods will at best detect only 70% of growth-retarded babies prior to delivery and in spite of constant refinement of current measurement techniques, ultrasound evaluation will only detect a few more. Lung maturation is thought to be at least partly determined by steroid production by the maturing fetal adrenal gland, a hypothesis supported by the role of exogenous steroids to assist lung maturation in prematurity. A prospective study of pregnant patients presenting for ultrasound after 24 weeks gestational age, for whatever clinical indication, was performed in which measurements of the adrenal gland were correlated with abdominal girth measurements and a ratio produced. This adrenal/abdominal ratio has been compared with clinical assessment of all babies to determine whether they were SGA or AGA. The results of the first 150 pregnancies will be presented.

Middle cerebral artery flow velocity waveforms obtained by colour flow imaging in appropriate and small for gestational age fetuses

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Colour flow imaging was used to identify the fetal middle cerebral artery for subsequent pulsed Doppler studies. In a cross-sectional study of 162 appropriate for gestational age fetuses (AGA) the pulsatility index (PI) of flow velocity waveforms (FVW) from the fetal middle cerebral artery fell with advancing gestation. The mean blood velocity in this vessel was also measured in 106 of these cases, and increased with gestation. In 48 small for gestational age fetuses (SGA) the PI of FVWs from the fetal middle cerebral artery was significantly lower, and in the 34 SGA cases in whom this was measured the mean blood velocity was significantly higher, than the AGA group. Fetal blood sampling by cordocentesis was performed in all SGA fetuses and a significant quadratic relationship was found between fetal hypoxemia and reduction in the PI of FVWs from the fetal middle cerebral artery. Thus, maximum reduction in PI is reached when the fetal pO_2 is 2–4 standard deviations below the normal mean for gestation. When the oxygen deficit is greater there is a tendency for the PI to rise, and this presumably reflects the development of brain oedema.

Transvaginal ultrasound in the serial assessment of the cervix in twin pregnancies

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There is an increased perinatal mortality rate in twin pregnancies compared with singleton pregnancies. This is principally due to a much higher incidence of preterm deliveries in twins compared with singletons. It is thought that changes in cervical length may predate the onset of preterm labour. The prediction of preterm labour by serial digital examination of the cervix has been attempted, but this has the disadvantage that manipulation of the cervix may cause the release of prostaglandins which are thought to play a part in the onset of labour. Abdominal ultrasound has been used to assess the cervix in singleton pregnancies, but visualization is poor and even more so in twin pregnancies because the presenting part may be low in the pelvis. By using the new technique of transvaginal ultrasound the cervix is easily visualized, and therefore it is possible to monitor changes in the cervix which will predate the onset of preterm labour. The cervix was assessed in 30 twin pregnancies using a 7.5 Mz transvaginal transducer fortnightly from 26 weeks onwards to delivery. In this paper the normal changes in the cervix in twin pregnancies are presented and the predictive value of the technique in the detection of preterm labour are discussed.

Placental localization using transvaginal ultrasound

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Whilst in gynaecological practice transvaginal ultrasound may complement the bimanual examination, its role in obstetric practice is yet to be established. This small pilot study describes the usefulness of this technique in the diagnosis of placenta praevia. Thirty patients admitted with antepartum haemorrhage had an abdominal scan and a transvaginal scan to establish placental site. All 30 patients have delivered and the results are presented. A 3.0 MHz mechanical sector transvaginal transducer with an effective focal range of 7.0 cm was used. Six patients were diagnosed to have major degrees of placenta praevia and these were confirmed by transabdominal scans and at delivery by Caesarean section. The diagnosis of a minor degree of placenta praevia was made in 10 cases but this was ruled out by transvaginal scans. In the remaining 14 patients placenta praevia was excluded by both techniques. There is no risk of provoking bleeding when using the transvaginal technique because the effective focal length of the transducer allows adequate visualization of the cervix and lower uterine segment with the transducer tip 2–3 cms into the introitus. Transvaginal ultrasound has advantages over transabdominal ultrasound. Firstly, the patients do not need a full bladder in order to see the lower uterine segment and secondly it overcomes the difficulties in visualizing the edge of a posterior placenta because of acoustic shadowing from the fetal head.

Gynaecological ultrasound

Chairmen: R. Goswamy and J. Morsman

Vaginal Doppler studies to assess uterine bloodflow in infertility—a new type of waveform analysis, by R. Goswamy
Vaginal versus abdominal ultrasound guided oocyte retrieval in IVF, by B. Rizk, C. Steer, S. L. Tan and B. A. Mason
Vaginal colour Doppler assessment of uterine impedance in a subfertile population, by C. Steer, B. Rizk, S. L. Tan, B. Mason and S. Campbell
Investigation of chronic pelvic pain in women: a comparison of venography and transabdominal pelvic ultrasound scanning, by T. Rae, R. W. Stones and R. W. Beard
Pelvic congestion in women: evaluation with transvaginal ultrasound and observation of venous pharmacology, by R. W. Stones, T. Tae and R. W. Beard
Transvaginal colour flow mapping—a novel technique for screening for ovarian cancer, by T. Bourne
Maternal dysfunction as the cause of ultrasound-induced fetal weight reduction in mice, by A. R. Williams and S. B. Barnett

Vaginal Doppler studies to assess uterine bloodflow in infertility—a new type of waveform analysis

R. Goswamy

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In previous studies I have described that Doppler studies of the uterine artery can be performed to assess uterine response to endogenous hormones during spontaneous ovarian cycles. Those studies were performed using a duplex system with a 3 Mz off-set pulsed Doppler transducer where scans were performed abdominally (Philips SDD 600 with Philips SDR1550). In the present study I wish to present data on Doppler studies performed with a duplex system using a 3 MHz on-line pulsed Doppler along with a 7.5 MHz imaging system, (Siemens SL2), where studies were performed vaginally to assess uterine response to endogenous hormonal changes in the ovarian cycle. Patients were scanned in the dorsal position. Oblique longitudinal scans were performed to image the ascending branch of the uterine artery at its point of entry just lateral to the cervix, using a 7.5 MHz imaging transducer. The pulsed Doppler gate was then placed where pulsations were seen and waveforms elicited by switching to the 3 MHz Doppler mode. Flow velocity waveforms were studied on at least three occasions during spontaneous cycles. The modified resistance index, modified S/D ratios and waveform classifications (Type O,A,B,C), as described in previous puplications, were noted at each examination. In addition, the ratio between the area under the systolic component (*S) and the area under the diastolic component (*D) was measured to calculate a new index, the Perfusion Index (PeI). This paper will compare the PeI with other forms of waveform analysis previously described and show that this is a superior index to assess end organ resistance. The clinical importance of assessing uterine response in infertile women will be emphasized to correct a postulated cause of infertility.

Vaginal *versus* abdominal ultrasound guided oocyte retrieval in IVF

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Four hundred and fifty two patients who underwent IVF treatment cycles and had transvaginal ultrasound guided oocyte retrieval were compared with 493 patients who had abdominal transvesical oocyte retrieval. The mean age of the patients in the two groups was similar (35.2 ± 0.7 *versus* 35.6 ± 0.9). The stimulation regimen in both groups were either cc/hMG or Buserelin/hMG. The major cause of infertility was equally distributed in the two groups. The mean number of oocytes retrieved was significantly higher (9.2 ± 1.4 *versus* 5.4 ± 1.2) and the length of the procedure shorter in the transvaginal group compared with the transabdominal group. One patient developed mild pelvic infection in each group. One patient developed frank haematuria in the abdominal group. The patients whose oocytes were retrieved via the transvaginal route were more comfortable when assessed by a five point scale. We conclude that transvaginal ultrasound guided oocyte retrieval is superior to transabdominal and should be routinely employed.

Vaginal colour Doppler assessment of uterine impedance in a subfertile population

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A decrease in uterine blood supply has recently been postulated to be a cause of female infertility. We have quantified changes in uterine artery perfusion by analysing Doppler flow velocity waveforms, obtained using a colour Doppler Vingmed CFM 700 with a 7.5 MHz vaginal probe. Changes in impedance were assessed by calculating the pulsatility index (PI). The PI was chosen as it most accurately expresses variations in the waveforms when there is an absence of end diastolic frequency shifts. We have previously quantified the changes in PI throughout the normal menstrual cycle and these values have been used to assess the variation from normal associated with infertility. Three groups of subfertile patients were selected: (1) 15 patients who had undergone unilateral salpingectomies for ectopic pregnancy; (2) 15 patients with unexplained infertility; (3) 15 patients with ultrasound evidence of polycystic ovaries. Our results have shown the following. (a) Scarring associated with the removal of a fallopian tube causes an associated increase in uterine artery impedance over that measured on the normal side. (b) Women with Polycystic ovaries have a decreased uterine artery impedance compared with that expected in a normal cycle. (c) Patients who have a low midluteal phase progesterone value have an associated increase in uterine artery impedance beyond the expected value. These results have demonstrated that uterine artery blood supply is altered outside the normal range as a consequence of pelvic pathology.

Investigation of chronic pelvic pain in women: a comparison of venography and transabdominal pelvic ultrasound scanning

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Venous congestion is recognized as an important cause of unexplained pelvic pain in women. Following clinical assessment, patients referred to the Pelvic Pain Clinic were investigated by transuterine venography. Transabdominal pelvic ultrasound scanning was initially employed in these patients to detect polycystic ovaries, a frequent association. In addition studies were undertaken to assess the uterine dimensions and endometrial thickness in pelvic pain patients compared with a normal population, and to validate these measurements against measurements made of surgical specimens at hysterectomy. Dilated pelvic veins were often observed during ultrasound scanning, but the significance of this finding in relation to venography has not been elucidated. In the present study ultrasound assessment of pelvic veins was compared with the results of the established venographic technique. A scoring system is used for evaluation of venograms which takes into account the ovarian vein diameters, the rate of disappearance of contrast medium and the degree of congestion. A similar scoring system for the ultrasound appearances of pelvic veins was devised to facilitate comparison of the two modalities. Thirty patients with chronic pelvic pain underwent transabdominal pelvic ultrasound scanning on an Acuson 128 duplex system, and transuterine venography on separate occasions. Pelvic veins were identified using real time ultrasound and confirmed as such with Doppler. The scoring system took into account the numbers of vessels seen, the maximum vein diameter, and an assessment of the overall appearances. 77% of patients had venographic evidence of pelvic venous congestion. Ultrasound agreed with venography as to the presence or absence of congestion in 22/30 (73%) of cases. These findings suggest that ultrasound scanning has a place in the imaging of pelvic veins in patients with chronic pelvic pain. The limitations of ultrasound compared with venography, particularly for the assessment of the reduced pelvic venous flow characteristic of these patients, are discussed.

Pelvic congestion in women: evaluation with transvaginal ultrasound and observation of venous pharmacology

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Pelvic venous congestion is a frequent finding in women with chronic pelvic pain. Treatment is with psychotherapy, progestogens, or the venoconstrictor agent dihydroergotamine (DHE). Dilated pelvic veins may be demonstrated by transuterine venography, which remains the standard imaging modality for diagnosis and for assessing the effects of treatment. However, venography is sometimes uncomfortable for patients and often requires sedation. Longer studies are limited by considerations of radiation exposure. Dilated pelvic veins may be observed using transabdominal ultrasound scanning but image quality is limited and the examination may be uncomfortable for the patient because of a full bladder. Spontaneous contractile activity of pelvic veins has been described *in vitro* but no *in vivo* data are available. Pelvic congestion remains a condition of unknown pathogenesis and an understanding of venoconstrictor and dilator mechanisms acting in the pelvic vessels is required. Transvaginal ultrasound scanning has the advantage of greater proximity to the pelvic vasculature, enabling high resolution imaging of dilated pelvic veins and their continuous observation under different physiological and pharmacological conditions. In the present study dilated pelvic veins in women with chronic pelvic pain were observed using continuous transvaginal ultrasound scanning of a single vessel. The effects of vasoconstrictor and vasodilator agents on venous calibre and blood flow were evaluated. DHE administration in seven patients resulted in a highly significant ($p < 0.002$) constriction in pelvic vein diameters. No changes were apparent in venous flow rates. Data are presented on spontaneous contractile activity in pelvic veins and venous dilatation following the infusion of vasoactive intestinal peptide (VIP).

Transvaginal colour flow mapping—a novel technique for screening for ovarian cancer

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Intraovarian vasculature and blood flow impedance has been analysed using transvaginal colour flow mapping. The aim was to refine the screening procedure for early ovarian cancer, allowing us to differentiate between benign and malignant ovarian cystic lesions.

The procedure was carried out on 42 selected women, in whom the presence or absence of coloured areas and the pulsatility index (PI) were recorded for all ovaries. Of the 30 women with morphologically normal ovaries the PI ranged from 3.1 to 9.4, and no areas of neovascularization were seen. In eight patients with a non-malignant mass seven had no signs of neovascularization and a PI value ranging from 3.2 to 7.0. One patient with bilateral dermoid cysts containing nests of thyroid cells had vascular changes and PI values of 0.4 and 0.8 respectively.

All five patients with primary ovarian cancer (four stage III and one stage Ia) had intratumoural neovascularization and low PI values ranging from 0.3 to 1.0. No significant vascular changes were seen in a patient with an intraepithelial serous cystadenocarcinoma within a small ovary (< 5.0 ml); the PI value in this case was 5.5.

These results suggest that transvaginal colour flow imaging may be used to help differentiate between benign and malignant ovarian lesions. As such it may be used to detect primary ovarian cancer, and help investigate the early stages of tumourogenesis. This technique is now being applied to our large scale ovarian screening trial. We feel that its routine application may be of great value in reducing the false positive rate of an ultrasound-based screening programme for ovarian cancer.

Maternal dysfunction as the cause of ultrasound-induced fetal weight reduction in mice

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Two independent research groups have established that the feti of mice exposed *in utero* to therapeutic intensities of ultrasound at an early stage of gestation were smaller at term than their non-exposed controls. One of these groups noted that some of the pregnant animals exposed to ultrasound had suffered neural damage (*e.g.* hind limb paralysis, HLP and/or distended bladder syndrome, DBS) but did not associate this maternal damage with an impairment of the conditions for the growth of the feti. We exposed pregnant mice during their eight day gestation under conditions where the 1.7 cm diameter (−20 dB beamwidth) ultrasound was centred mid-way between the two horns of the uterus so that its contents received virtually no direct exposure. It was found that the feti from animals exposed to 1–5 W/cm^2/SATA ultrasound but which showed no evidence of HLP or DBS were indistinguishable from those of the control group. However, the feti from animals which developed HLP and/or DBS following ultrasound exposure were significantly smaller than their controls. It was also found that the increase in maternal weight at necropsy on day 17 or 18 was significantly less for those animals which developed HLP or DBS than for the control animals or the ultrasound-exposed animals which showed no evidence of neurological damage. It is therefore apparent that the observed fetal weight reduction results from maternal compromise and is not the result of direct effect of ultrasound on the fetus.

Physics and instrumentation

Chairmen: M. Halliwell and M. Casebow

Reduction of speckle noise in clinical ultrasound images: a fast implementation for clinical application, by D. C. Crawford, D. S. Bell, D. O. Cosgrove and J. C. Bamber
Formulation of wave–equation migration for medical ultrasound image enhancement, by W. A. Sandham and J. L. Bowie
A comparison of the Doppler spectra from human blood and artificial blood used in a flow phantom, by P. R. Hoskins, T. Loupas and W. N. McDicken
Electronic system for quality assurance of Doppler equipment, by J. A. Evans and R. Price
An ultrasonic echo microscope for imaging and measurement of superficial tissues, by C. M. Moran and J. C. Bamber
Acoustic properties of lesions generated with an ultrasound therapy system, by N. L. Bush, J. C. Bamber, I. Rivens and G. R Ter Haar
Measurement of the velocity and attenuation coefficient of ultrasound in bone, by D. K. Nassiri, K. Edmunds and A. Britten
Two case studies in ultrasound exposure measurement, by F. A. Duck

Reduction of speckle noise in clincial ultrasound images: a fast implementation for clinical application

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Early experience of new forms of adaptive filtering for ultrasound speckle reduction and parametric imaging, using off-line conventional digital processing, has been sufficiently encouraging to warrant attempts to build fast on-line implementations for purposes of clinical trials. The hardware and software development will be described briefly and results of clinical trials will be presented. Logarithmic compression and other processing within commercial ultrasound systems distorts the echo-amplitude histogram obtained from the video image and hence the statistical properties of the speckle noise. We have been able to compensate for this effect by applying an inverse transform to the digitized video image. A number of methods for adaptive smoothing of speckle noise, using local statistics to determine regions of speckle, are currently under investigation. One statistical feature used is the second moment, M2 ($= \langle x^2 \rangle / \langle x \rangle^2$). Off-line floating point calculations have demonstrated that by applying the inverse transform prior to calculation of the M2 parametric image there is a marked improvement in the uniformity of M2 values, and a reduced dependence of M2 on the mean echo-amplitude, for speckle regions. Adaptive smoothing of speckle noise in a clinical setting requires high speed processing. The M2-based algorithm has been implemented on a commercial image processor. This device, however, performs calculations with limited precision which leads to introduction of artefacts into the parametric image and difficulties with implementing the inverse transform. An alternative to applying an inverse transform to the input image, which eliminates these artefacts, is to use the variance/mean as the statistical feature. The variance/mean parametric image possesses the same desirable characteristics as those exhibited by the M2 parameter calculated using the floating point implementation and the inverse transform. Results of the clinical evaluation of speckle noise filter will be demonstrated by illustrations of the original and processed ultrasound images recorded during clinical abdominal and breast examinations.

Formulation of wave-equation migration for medical ultrasound image enhancement

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Substantial advances in diagnosis via medical ultrasound have resulted from improvements in spatial resolution, achieved by beamwidth reduction using techniques such as focusing and aperture synthesis. As the limit of these techniques is approached, further enhancement of the image is possible only by employing some form of post-acquisition data processing, such as migration. This is an image enhancement technique used during the processing of seismic exploration data, which removes in some optimum sense the propagation effects of the sub-surface, placing reflectors at their correct positions and collapsing diffractions. The majority of migration techniques are based on the acoustic wave-equation, and involve a two-step procedure: downward continuation of the wavefield recorded at the surface, followed by an imaging step. Although the nature of the medium and the data acquisition technology differs vastly between seismic exploration and medical ultrasound, there is a great deal of similarity between the two disciplines regarding a theoretical description of propagation of the wavefield in the two media. The seismic migration equations may therefore be reformulated to enhance medical ultrasound images, obtained from either linear array transducers or for sector scans. This paper indicates how artifacts on ultrasound images may be caused by the finite beamwidth effects of the transducer and also from sidelobes. The basic principles of migration are then reviewed together with some of the more popular migration methods currently used in the seismic exploration industry. These are illustrated briefly with examples. The migration equations are then reformulated for medical ultrasound images, and a method shown by which an ultrasound image may be enhanced using the reformulated migration equations.

A comparison of the Doppler spectra from human blood and artificial blood used in a flow phantom

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The characteristic speckle pattern seen on the Doppler spectrum from Fourier transform based spectrum analysis arises as a result of the fluctuation in red cell concentration in the sample volume. In a flow phantom it is very inconvenient to use blood as the scattering medium. Commonly a blood substitute such as a suspension of Sephadex G-25 particles is used. These particles have a smaller diameter of 20–70 μm which is much larger than the red cell dimensions of approximately 2.4 × 8.5 μm. In this study the backscattered Doppler power and the statistics of the Doppler spectrum were measured for human blood and a suspension of Sephadex G-25 particles. It was found that the first and second order statistics of blood and the Sephadex suspension were very similar. The statistical parameters were independent of Sephadex concentration, suggesting that no special measures need to be taken to ensure a suspension of the correct concentration. The relative Doppler power from blood was lower than the backscattered power from Sephadex by a factor of 150–250.

Electronic system for quality assurance of Doppler equipment

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A system for testing the Doppler equipment has been developed, based on the concept of electronic signal injection similar to that used in the ASIST device for imaging machines. The machine under test is coupled via a perspex block to the testing device. After amplification to a standard level using automatic gain control this signal is fed to a mixer where it is mixed with a local oscillator signal of about 1 kHz. The mixer output containing this simulated Doppler shift is fed back via another transducer to the Perspex block and hence to the machine under test. The Doppler shift simulated is precisely known and controlled and does not depend on the frequency of the machine under test. The Perspex block produces a known delay which, in the case of pulse Doppler machines, can be used to test the range gating accuracy. An estimate of system sensitivity can also be obtained. The equipment is cheap, portable and can be used on almost any Doppler equipment without removal of equipment covers. It is therefore a good "first-line" quality control tool which complements more sophisticated flow phantoms.

An ultrasound echo microscope for imaging and measurement of superficial tissues

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As a measurement system for studying the acoustic properties of skin, and as a laboratory prototype of a high resolution B-scan imaging system for eventual application in dermatology and surgical oncology, a scanning acoustic microscope operating at frequencies up to 60 MHz has been developed. The design of high-frequency spherically focused transducers, built into mini BNC connectors, provides a consistent electrical impedance and compact lightweight units suitable for rapid mechanical scanning. A number of such transducers have been made with focal lengths in the range 3–7 mm, the upper limit being constrained by the dimensions of the connector. Two types of piezoelectric film were employed in transducer manufacture: PVDF and the co-polymer P(VDF-TrFe), the latter giving about three times the sensitivity of the former (with a round trip sensitivity of the order of −43 dB for a perfect reflector at the focal distance). The transducer is mechanically scanned in two dimensions using optical precision linear stepping drives. The sample is mounted on a quartz flat in a water tank which is in turn mounted on a high precision jack to allow the distance between the transducer and sample to be adjusted. All movements are under computer control. For B-scans, C-scans and backscatter measurements the transducer is focused within the sample. Otherwise, for attenuation and velocity measurements, it is focused on the quartz flat. The corresponding echo signals are digitized at 200 MHz to 8 bits and stored in sufficient fast memory to hold data for a complete B-scan before it is necessary to transfer it to the computer, thus facilitating short scan times for the elimination of movement artefact in living subjects. Image data is displayed on a 512 by 512 pixel by 8 bit frame store. Digitizing the signal immediately following a linear amplifier which has computer-controlled gain and offset level provides a mode of operation suitable for quantitative measurements, and permits alternative signal processing schemes to to be tried in software. For static subjects a wide dynamic range signal may be reconstructed from multiple scans taken at different gain settings, and control of the offset level permits either r.f. data to be digitized or fast half-wave rectification to be accomplished. Alternatively, analogue compression and envelope detection allow a higher maximum operating frequency and rapid B-scan capture.

Acoustic properties of lesions generated with an ultrasound therapy system

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We have previously described apparatus and techniques developed for quantitative imaging of the ultrasound propagation and histological properties of spatially inhomogeneous sections of excised tissues. This paper reports the results of applying these methods to the examination of the acoustic structure of lesions in liver tissue which have been created by means of high power ultrasound. Controlled local destruction of tissue by remote high power focused ultrasound is being studied with a view to eventual clinical use in the treatment of cancer, particularly liver metastases. Knowledge of the manner in which the acoustic propagation properties of treated tissue are altered relative to surrounding untreated tissue is important in understanding (a) the mechanisms by which already treated regions can distort the acoustic dose distribution in the treatment beam and (b) the processes which contribute to the acoustic contrast that will enable a diagnostic ultrasound imaging system to visualize the lesions during interactive control of the treatment. Single lesions, approximately 1 cm in diameter and 3 cm long, were created in five specimens of fresh pigs liver. From each of these a section, 3 cm by 3 cm by 7 mm, was cut centrally through the lesion and in a plane perpendicular its long axis, resulting in a lesion of approximately circular cross-section surrounded by normal liver and passing through the complete thickness of the tissue section. The mounting and measurement procedure, which will be described briefly, results in two-dimensional images of sound speed, attenuation coefficent as a function of frequency in the range 3–8 MHz and backscatter coefficient over a similar frequency range. Regions within these images were then defined so as to obtain good averages of the properties for the lesion and for the untreated liver. Line profiles through the images indicate the homogeneity of the properties within the lesions and the rate of change at the lesion margins. The results indicate that sound speed in liver is slightly elevated (by about 0.7%) in treated tissue, and both attenuation and backscatter are substantially increased (170–100%). Degassing studies were used to demonstrate that these changes in acoustic properties are associated with alterations to the tissue components rather than being due to bubbles generated by the treatment beam.

Measurement of the velocity and attenuation coefficient of ultrasound in bone

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This paper reports on the development of a dedicated system for measuring the velocity and attenuation coefficient of ultrasound as a function of frequency in small specimens. The system uses two 8 mm diameter aperture matched polyvinylidene fluoride (PVDF) probes focused at 35 mm. The transducers are placed at a fixed distance of 71 mm from each other in two sealed containers each with a thin rubber membrane of 0.15 mm thickness acoustic window. One of the containers can be moved in order to place the specimen between the transducers. Both transducers can be moved simultaneously in the vertical direction so that the specimen can be scanned in order to achieve correct positioning and an adequate number of measurements for averaging. Electrical pulses with repetition frequency of 1–500 Hz controlled by the microcomputer are produced at the transmitter output. These pulses can excite both transducers. The received echoes from either transducer are pre-amplified and, via a calibrated attenuator and second amplifier, are routed to an oscilloscope and a 48 MHz 8 bit analogue-to-digital convertor. The gated digital signals and their time of arrival are used to calculate the thickness of the specimen, the velocity in the specimen and the attenuation coefficient of sound in the specimen. Twelve cancellous bone specimens were prepared and their velocity and attenuation coefficient were measured using the above system. The results of the measurements were correlated with the mineral content measured using dual X-ray photodensitometry and chemical analysis of the specimens. The clinical application of this acoustical technique for diagnosis and monitoring of bone development in pre-term infants are discussed.

Two case studies in ultrasound exposure measurement

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During the past 18 months ultrasound exposure measurements carried out on installed diagnostic ultrasound equipment have revealed two circumstances of particularly high ultrasonic output from imported duplex scanners operating in pulsed Doppler mode. For one mechanical sector scanner, it was found that spatial peak temporal average intensity (I_{SPTA}) in water could reach 10 W cm^{-2}. On a second, phased array, scanner it was found that power dissipation in two transducers could cause their surface temperature to exceed 60°C. In each case both the UK agents for these companies and the Department of Health were informed. As a result, both companies have altered the electrical drive conditions to their transducers so that they now operate within the relevant regulation. In the first case the intensities have been reduced below those required in the USA by the Food and Drug Administration (FDA). In the second case, the maximum operating temperature of the transducers has been reduced to 41°C, as required by British Standard BS5724. The role of regulations in controlling ultrasonic output are discussed, and the lack of regulations relating to the sale of diagnostic ultrasonic equipment in the UK are noted.

Orthopaedic teach-in

Chairman: S. Scott

Ultrasound assessment of fracture healing, by J. L. Cunningham and C. J. Kershaw
Assessing fracture union using ultrasonic velocity measurements, by I. N. Mawhinney, P. J. Gill and R. A. B. Mollan
Why is congenital dislocation of the hip rare in Chinese? by Y. L. Chan, J. Cheng and C. Metreweli
A prospective study of hip fracture in an elderly residential population, by R. W. Porter, D. Grainger, S. Palmer and C. Miller
Sonographic diagnosis of acute anterior knee swellings in adults, by W. W. Gibbon and H. Mamtora
Sonographic assessment of acute collateral ligament injuries to the ankle, by W. W. Gibbon and H. Mamtora
The role of diagnostic medical ultrasound in the management of hand injuries, by D. D. McGeorge and S. E. McGeorge

Ultrasonic assessment of fracture healing

J. L. Cunningham and *C. J. Kershaw

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The velocity of an ultrasonic wave across a discontinuity in a structure, such as a fracture, can be used as a measure of healing if compared with the velocity in the continuous structure, *i.e.* the unfractured contralateral bone. The bones most suitable to measurement are those with a thin covering of soft tissue and in this study fracture healing has been monitored in a group of tibial fracture patients. Testing is carried out with the patient in a supine position. Two measurement points, a known distance apart, are marked, one either side of the fracture, the same position of points being used on the unfractured tibia. A commercially available ultrasound unit, normally employed in the non-destructive testing of concrete, was used for the testing (PUNDIT, CNS Electronics Ltd). Two 1 MHz ultrasound transducers were used; these were hand-held on the measurement points and the ultrasound transmission time noted. The ultrasound velocity was calculated from the transmission time and the known distance between measurement points. To date, 15 patients with closed tibial fractures have been monitored using this technique. The ultrasound velocity in the fractured tibia approaches that of the unfractured tibia as healing progresses. At the point where the fracture is judged (by manual manipulation and X-ray) to be clinically healed, the ultrasound velocities are coincident. Where fracture healing is delayed, the ultrasound velocities are slower to become coincident, thus reflecting the delay in healing.

Assessing fracture union using ultrasonic velocity measurements

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There still lacks a scientific method of non-destructively monitoring fracture healing, and reliably assessing the strength of union. Research into various techniques such as vibrational, deflectometry and radio-isotopic has produced little success. Ultrasonic methods were briefly investigated in the past, but the trials were poorly controlled, and only used the low ultrasonic ranges. Sequential animal studies were performed investigating the ability of pulsed ultrasonic velocity measurements measured longitudinally along the bone across a fracture to monitor fracture healing. The pattern of change of the velocity as the fractures healed was compared with post-mortem mechanical testing. In a study using an external fixator to maintain the reduction of a mid-shaft osteotomy of rabbit tibiae, a reproducible pattern of change was noted. This pattern involved a rapid fall at the time of fracturing, a period of no change or slow rise, then a period of a rapid rise in velocity, and a final period of further slow rise in velocity towards the pre-fracture velocity. Delayed union and non-union models were created and different patterns of change were seen. Mechanical testing showed that if the rapid rise phase was not completed then failure was in a plastic manner with low stiffness and low load at failure, but if the rapid rise phase was completed then failure was in a brittle manner, with high stiffness with increasing load as further healing occurred. The correlation coefficient between the ultrasonic velocity and stiffness at failure was 0.84. In the delayed union fractures there was a significant difference from that of normal union in the load at failure and stiffness, reflecting the different pattern of ultrasonic velocity change.

Why is congenital dislocation of the hip rare in Chinese?

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Congenital Dislocation of the Hip (CHD) is relatively rare in Chinese. This has been attributed to the traditional Chinese manner of baby-carrying by mothers. If this is true then more cases of CDH will occur in the Chinese as the Western lifestyle becomes more pervasive. Conversely CDH could be reduced in the West by the adoption of Eastern practices. We have used Reinhard Graf's technique and classification to study 100 Chinese newborn hips to establish whether the hips are inherently more "stable" than those of German children and whether the diminished frequency of CDH is more related to nature than nurture.

A prospective study of hip fracture in an elderly residential population

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Doncaster Royal Infirmary, Hull Royal Infirmary and Warwick University

Retrospective studies of hip fracture suggest that osteoporosis is a significant risk factor, but the propensity to fall and the neuro-muscular response may be equally important. We have conducted a prospective study of a population of residential elderly women, to assess the relative importance of osteoporosis, cogniscence and mobility in the risk of subsequent fracture. **Method.** Women over 70 years of age in local authority and private residential care in Doncaster and Hull were assessed for osteoporosis using a new technique of ultrasound attenuation of the os calcis, for cogniscence by the CAPE test, and for mobility. We recorded subsequent fracture of the hip over a 2 year period. **Results.** 1444 women entered the study. There was no significant difference in the age, ultrasound attenuation, CAPE test and mobility for the 765 women in Doncaster and the 679 women in Hull. Thirty-eight women in Doncaster and 37 women in Hull fractured the hip in the 2 year period. There was significant difference in the ultrasound attenuation ($p < 0.001$), CAPE test ($p = 0.0016$) and mobility ($p = 0.035$) between the fracture and non-fracture populations. A discriminant analysis showed that ultrasound attenuation and the CAPE test were the most helpful predictors for subsequent fracture. The fracture rate of the 135 women who were neither osteoporotic nor of poor cogniscence was 2.22%, for 115 osteoporotic women of good cogniscence 2.60%, for 91 not osteoporotic but of poor cogniscence 4.40% and for the 108 osteoporotic women of poor cogniscence 12.4%. **Conclusions.** Osteoporosis as measured by ultrasound attenuation through the os calcis was the best predictor of hip fracture. The CAPE test, which contains a section on psychomotor coordination, and may reflect a propensity to fall, was also useful. Preventing osteoporosis should reduce the incidence of hip fracture, but measures to prevent falls in the elderly osteoporotic should also be productive.

Sonographic diagnosis of acute anterior knee swellings in adults

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The sonographic appearances of patella tendonitis and pre-patella bursitis have been recognized for some time. A recent paper also demonstrated well the ultrasonographic features of Osgood–Schlatter and Sinding–Larsen–Johanasson disease in adolescents. The object of the present study was to investigate the role of ultrasound in distinguishing acute from chronic pathology in tender and apparently acute, anterior knee swellings in adults. We excluded all cases where the swelling had been present for greater than 4 weeks prior to examination or where the swelling was clinically within the skin or immediate subcutaneous tissue. Twelve consecutive referrals from the Accident and Emergency Department, Hope Hospital, Salford fitting within the above protocol were examined sonographically at the Salford Royal Hospital using a high definition Acuson system with 5 MHz linear array transducer. A gel block sonographic stand-off medium was utilized if local pressure to the swelling was likely to elicit pain. The study group consisted of 10 male and two female patients of age range 30–73 years. All patients were also examined radiographically using standard AP and lateral projections. We were able to distinguish: (1) pre-patella bursitis from acute haemorrhage into the pre-patella bursa or soft tissues of the anterior knee; (2) acute from chronic patella tendonitis; (3) pre-patella from intrascapsular fluid collection. In addition we were able to diagnose a case of adult onset Osgood–Schlatter's disease in a 30-year-old and proximal tendonitis associated with pre-patella bursitis. In most cases of chronic disease changes were also present in the contralateral knee. We have found ultrasound examination to be a useful adjunct to clinical examination in all 12 cases providing information that was not available clinically or radiographically.

Sonographic assessment of acute collateral ligament injuries to the ankle

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Acute collateral ligament injuries to the ankle represent one of the most common presenting injuries to an Accident and Emergency Department. The clinical problem arises in identifying those cases with potential instability requiring adequate immobilization or even primary surgical repair in an attempt to avoid recurrent instability problems. We have compared the appearances of 12 acute de novo and 12 acute or chronic collateral ligament injuries using either 5 MHz linear array or 7.5 MHz sector scanners with high definition Acuson or Diasonics systems. A gel block stand-off medium was used if local pressure to the injured region was likely to be painful or if swelling was minimal at time of examination. We were able to demonstrate: (1) acute tears in the individual components of the lateral triradiate collateral ligament, *i.e.* anterior and posterior talo-fibula and calcaneo fibula ligament as well as the medial deltoid collateral ligament; (2) chronic changes in the anterior talo-fibula and calcaneo fibula ligaments—the chronically injured ligament was generally hypoechoic compared with the normal ligament and occasionally the hyperechoic central line of scar tissue could be observed; (3) avulsion fractures of bony ligamentous attachments or fifth metatarsal base and ability to distinguish recent from old bony injury; (4) associated haemarthritis with lifting of the anterior fat pad/capsule; (5) extent of superficial oedema and distinguishing acute from chronic ankle oedema. All cases were compared with plain AP and lateral radiographs. We found ultrasound useful in the evaluation of injury severity by demonstrating bilateral ligament tears with consequent potential instability. It was also able to distinguish acute from chronic injuries.

The role of diagnostic medical ultrasound in the management of hand injuries

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With the greater use of high frequency transducers, real time sonography uniquely provides the ability to study the complex anatomical structures of the hand. Non-invasive diagnosis of problems can be made and the results of surgery assessed. Tendon repairs can be monitored and their functional quality checked: indeed, collateral ligament and volar plate injuries can be diagnosed. Complications of surgery are easily identified with the potential for early intervention, obviating the need for lengthy and expensive secondary reconstruction. Presented is the normal ultrasonic anatomy of the hand and the versatility of the technique in the diagnosis and management of hand problems in clinical practice. The normal appearance of tendon repairs is demonstrated as well as the more common complications. In addition, other injuries not demonstrable by conventional radiography are presented.

Cardiovascular ultrasound

Chairmen: G. Leach and N. Dewhurst

Echocardiography in crush injury to the chest, by D. R. Naik, S. Tennant and G. Clark
Colour Doppler Evaluation of prosthetic heart valves in the immediate post-operative period, by C. Occleshaw, S. Tennant, A. Hampshaw and D. R. Naik
Is post mastectomy lymphoedema all lymphatic? pulsed and colour Doppler suggest a venous component, by W. E. Svensson, C. Badger, D. O. Cosgrove and P. Mortimer
Duplex Doppler ultrasonography—an effective and cost-effective alternative to contrast venography? by D. J. Widdowson and C. H. Wright
Colour Doppler ultrasound in deep venous thrombosis: a comparison with venography, by G. M. Baxter, S. McKechnie and P. Duffy
Angiography emulation using ultrasound—its value prior to percutaneous arteriography, by N. M. DeSouza, D. H. King, P. Pilgrim, P. Bates, J. F. Reidy and R. G. Gosling
Does pulse generated run-off accurately predict calf vessel and pedal arch patency prior to femoro-distal bypass? by M. G. Wyatt, R. M. Muir, W. G. Tennant, D. J. A. Scott and M. Horrocks
Duplex derived hyperaemic flow in the assessment of "at risk" femoro-distal grafts, by M. G. Wyatt, R. M. Muir, W. G. Tennant, D. J. A. Scott, R. Skidmore and M. Horrocks
Effect of treatment on carotial plaque size, by A. D. White, G. C. Carolan, J. P. Woodcock and M. S. J. Pathy

Echocardiography in crush injury to the chest

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Myocardial contusion is a recognized and potentially serious complication of blunt chest trauma. Despite the use of established and widely available diagnostic methods such as radionuclide scans, electrocardiography and cardiac enzyme estimation, its diagnosis and management have proved difficult. Two-dimensional echocardiography is capable of demonstrating changes in cardiac size and function rapidly and accurately. Previous studies have shown it to be a reliable predictor of myocardial damage. We report our experience of this condition in patients admitted to hospital as a result of the major disaster at Hillsborough Football ground in Sheffield. Of the 93 patients brought to the Casualty Department, 11 were admitted to the Intensive Care Unit. Two patients had signs of significant neurological damage and were excluded from this study. Echocardiography was carried out on nine patients within 24 h of admission. All patients had relevant radiographs, ECG and estimation of cardiac enzymes (OPK and CKMB). Echocardiography using cross-sectional views in parasagittal, short-axis and coronal planes together with colour Doppler was carried out and chamber size, wall-motion abnormalities, valvular regurgitation and left ventricular function assessed. The changes observed included wall-motion abnormalities, pericardial effusion, right ventricular enlargement and tricuspid regurgitation. Detailed results together with relevant clinical findings are presented and discussed. These results confirm the value of echocardiography in myocardial contusion.

Colour Doppler evaluation of prosthetic heart valves in the immediate post-operative period

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Early prosthetic valve dysfunction can be diagnosed by Doppler echocardiography. Many authors have emphasized the value of comparison with a baseline Doppler study for each individual patient in this situation. Yet, the majority of studies which show "residual" gradients across such prosthetic valves appear to have been carried out on patients some months or years after the surgery. It is also important to have baseline information on both the type of the valve and its size. In a prospective study we have carried out colour Doppler examinations on patients undergoing valve replacement in the immediate post-operative period. The prosthetic valves used at our hospital include three new types for which no published reports of "normal residual" gradients are available. Results of 100 such examinations are presented. In our study, the post-operative examinations also include pressure measurements both at rest and after exercise. The technique of the examination will be described and the importance of baseline examinations in the immediate post-operative period both at rest and after exercise are discussed. Data on the three new types of valve are also presented.

Is post mastectomy lymphoedema all lymphatic? pulsed and colour Doppler suggest a venous component

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Nineteen patients with a chronic swollen arm were examined with pulsed and colour Doppler. Sixteen had had a previous mastectomy or lumpectomy for breast cancer followed by radiotherapy, one had had a previous axillary clearance for metastatic melanoma and one a previous venous cannulation in the forearm. In one case no cause for the swelling was apparent. Conventional duplex pulsed Doppler showed changes in the venous flow pattern in 13 patients with indications of venous obstruction. Colour Doppler in five patients showed occlusion of the axillary or subclavian vein. These diagnoses were confirmed by the demonstration of abnormal venous drainage in the region of the origin of the subclavian vein with collaterals, often multiple, using colour Doppler. Colour Doppler was used to demonstrate the venous anatomy in the second part of the study; it clearly demonstrated venous collaterals which were not visualized using state-of-the-art conventional equipment. Our findings indicate that venous occlusion or obstruction is commonly associated with the post mastectomy/radiotherapy swollen arm. Observation in one patient and the known delay in its development suggest that the venous component of the swelling may occur some time after the treatment. This study suggests that the post mastectomy/radiotherapy swollen arm commonly has more than one aetiology and in many cases is due to a combination of venous and lymphatic obstruction; the common title "lymphoedema arm" is an oversimplification.

Duplex Doppler ultrasonography—an effective and cost-effective alternative to contrast venography?

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Contrast phlebography remains the accepted method of detection of venous thrombosis. Recent publications indicate that duplex Doppler ultrasonography (a combination of compression ultrasonography and Doppler venography) may provide an equally reliable method in the detection of venous thrombosis and have questioned the value of continuing routine venography. For any such non-invasive examination to be widely accepted it must be reliable, easily learned, repeatable and easily reviewable. The combination of direct imaging by real time ultrasound and duplex Doppler seems to offer this possibility. The introduction of non-ionic contrast media has reduced the incidence of complications in intravenous phlebography, but has added considerably to the cost. Adverse reactions to the contrast medium may still be experienced, and it may not be possible to perform the examination on a swollen oedematous foot. Although the ultrasound examination is reportedly complication free, the cost in capital investment and time of this method of diagnosis needs to be accurately assessed and compared with that of venography. Seventy-nine patients suspected of having deep venous thrombosis have been examined by ultrasound to date in our department, using a commercially available real time scanner with Doppler facilities. In 70 patients, contrast venography was performed concurrently (a swollen foot and/or unobtainable veins precluding contrast examination in the remaining nine cases), and in the majority of these cases, the ultrasound examination was performed without knowledge of the results of the contrast study. Thirty-five cases were deemed positive by a combination of both techniques; in two of these cases venography was not possible and in a further two the findings were equivocal. Four of the ultrasound examinations failed to show significant thrombus. In a small number of cases ultrasound provided useful additional information, but in a significant number of cases the examination was found to be difficult and time consuming. The findings will be presented in detail and the technical difficulties experienced discussed in an attempt to clarify the cost and the role of the two techniques in a District General Hospital setting. This project was supported by the Du Boulay Trust.

Colour Doppler ultrasound in venous thrombosis: a comparison with venography

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Venography is widely accepted as the imaging gold standard in cases of suspected deep venous thrombosis of the lower limb. Because of the possible danger of contrast reaction and local endothelial toxicity, non-invasive methods have been assessed, *e.g.* impedance plethysmography and fibrinogen scanning, many of which have major drawbacks. A number of recent studies using real time ultrasound have shown good correlation with venography in the femoral and popliteal segments, although on occasion the extent of thrombus formation has been underestimated. To date, no reliable estimation of calf vein patency has been made. In our study, a double blind prospective study of 40 patients (age range 20–70 years), direct comparison was made between venography and colour Doppler imaging using a 5 MHz linear array probe (Acuson 128). With the patient in a supine position, the femoral vein was visualized throughout its length in both a transverse and longitudinal axis down to the level of the adductor canal. Turning the patient into a lateral position with the knee flexed approximately 25°, the popliteal segment and calf veins were visualized. Assessment of venous patency was based on response to probe compression, intraluminal echogenicity, presence of venous waveform with effects of distal compression (at femoral and popliteal levels), and colour flow assessment. Response to Valsalva manoeuvre was not included. The results and limitations of this technique are available for discussion.

Angiography emulation using ultrasound—its value prior to percutaneous arteriography

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The prevalence of peripheral vascular disease demands a quick, reliable non-invasive technique for initial assessment. We have devised a new method which combines two physical principles: (1) Doppler shift and blood velocity, (2) blood velocity inversely and arterial cross-section with the ability to track probe position using a non-contacting method. An image of the probe track and any arterial narrowing is shown superimposed on an outline of the patient. Pressure measurement, scan and graphics with final report take 20 min. We have evaluated the accuracy of this system in peripheral vascular disease. Thirty-one patients under went quickscan (QS) and then arteriography within an average time of 7 days. Abdominal aorta, common iliac–common femoral, superficial femoral and popliteal artery segments were graded indpendently as normal, significant stenosis ($>$ 50% of diameter) or occluded by both techniques. Of 197 segments, QS correctly assessed 110 normal, 22 stenosed and 26 occluded segments. Four equivocal angiographic stenoses were normal on QS and four severe stenoses were graded occlusion. Fifteen segments on angiography and five on QS were not assessed. For the iliac and superficial femoral artery segments, sensitivity and specificity averaged 82% and 90% respectively for all grades. Aortic statistics were invalid (only one significant lesion). Six out of eight popliteal occlusions were correctly diagnosed by QS, but no popliteal stenoses were detected out of six shown on arteriography. This contrasts with a separate study on femero-popliteal grafts using the same protocol, where three out of four distal anastomoses/popliteal stenoses were confirmed by QS. Low numbers may contribute to this discrepancy but improved popliteal scanning method may be necessary. Initial QS work-up has been used over the last 2 years at Guy's Hospital to direct percutaneous angiography and indicate potential sites for angioplasty.

Does pulse generated run-off acurately predict calf vessel and pedal arch patency prior to femoro-distal bypass?

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Pedal arch patency may be an important factor in the success of femoro-distal grafts. The pre-operative assessment of both calf vessel and pedal arch patency is often poor using conventional arteriograms, but can be improved with the use of intra-arterial digital subtraction arteriography (DSA). Pulse generated run-off (PGR) is a non-invasive method of determining calf vessel patency, but may also be used in the assessment of the pedal arch. It is based on a standard 10-MHz Doppler ultrasound velocimeter and a sphygmomanometer cuff driven by compressed air. The cuff is placed around the upper calf and pulsatile pressure develops blood flow in calf and arch arteries, even if the resting Doppler signal is inaudible. The aim of this study was to compare the accuracy of PGR and pre-operative DSA in the prediction of calf vessel and pedal arch patency prior to distal reconstructive surgery. Thirty-five patients undergoing femoro-distal bypass for critical ischaemia were studied. Each underwent a PGR examination and a pre-/and post-operative DSA. On arteriography, each calf vessel was scored as fully patent (2), diseased (1) or occluded (0) and the pedal arch as complete (2), incomplete (1) or occluded (0). PGR scores of 2 or 1 were given to each calf vessel with a biphasic or monophasic waveform respectively and the pedal arch scored as for arteriography. There was no correlation between the PGR scores and the pre-operative DSA. There was, however, an excellent correlation between the PGR and the post-operative DSA, for both calf vessel (rs = 0.96, $p = 0.002$) and pedal arch (rs = 0.62, $p = 0.008$) patency. These results confirm the value of PGR in the pre-operative assessment of both calf vessel and pedal arch patency. Reliance on pre-operative arteriography alone will invariably underestimate the status of reconstructable distal vessels and may lead to unnecessary amputations.

Duplex derived hyperaemic flow in the assessment of "at risk" femoro-distal grafts

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The identification of failing femoro-distal grafts has been investigated in 40 patients using duplex derived volume flow measurements, at rest and following reactive hyperaemia. Resting flow was measured at mid thigh level (mean of three readings). Two hyperaemic stress tests (I = an occlusive cuff 50 mmHg above systolic pressure for 2 min; II = active ankle plantar-dorsiflexion for 2 min) were assessed and the results expressed as the mean percentage rise from the resting value +95% confidence interval. An intra-arterial digital subtraction arteriogram was performed on each patient and the grafts defined as "at risk" or control dependent on the presence or absence of graft or run-off stenoses.

Results	Controls	"At risk"
Patient number	22	18
Mean resting flow (Q)	122 + (87–157)	161 + (115–207)
Test I (% rise Q)	647 + (343–950)	169 + (85–253)^a
Test II (% rise Q)	434 + (51–816)	149 + (60–238)^b

$^a p < 0.001$, $^b p < 0.05$—Mann–Whitney U test.

There was no significant difference between the resting flow in the control and the "at risk" groups. There was, however, a significant difference between the two groups following both hyperaemic stress tests. A hyperaemic flow increase of greater than 200% was able to predict "at risk" grafts with a sensitivity and specificity of 100% and 78% for test I and 53% and 53% for test II respectively. These results show that whereas resting flow volumes are similar, the use of a hyperaemic stress test is able to distinguish between control and "at risk" grafts. The 2 min cuff hyperaemic test is simple to apply and is superior to active ankle flexion. It may help to identify "at risk" grafts before they fail.

Effect of treatment on carotid plaque size

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Stroke may result from embolization of atheromatous plaque in the carotid arteries. Rational treatment to prevent this is difficult since the natural history of carotid plaque is unclear. Most carotid plaques remain unchanged over time. Some plaques progress and others regress, but little is known about the influence of drug treatment on such variations. Ultrasound studies were carried out on patients who had been referred for investigation of cerebrovascular disease. The degree of stenosis was estimated according to standard criteria. Those patients who had more than one examination were selected for this study. In each case, note was made of the presence or absence of drug therapy and this was correlated with change of plaque size in each vessel except where surgical treatment had been carried out. Over 3 years, 131 patients had 160 serial examinations. The reason for the repeat was: review in 77 cases; new acute cerebral ischaemic event in 20 cases; post endarterectomy study (unoperated side) in 29; postEC/IC bypass in five cases. In the review cases ($\chi^2 = 0.3088$, $p > 0.5$), cases following acute cerebral ischaemia ($\chi^2 = 1.944$, $0.1 < p < 0.5$), and post-endarterectomy (unoperated side) ($\chi^2 = 0.689$, $0.1 < p < 0.5$) there appeared to be no significant difference in the progression or regression of the plaque between the treated and untreated groups. A significant effect by a single drug is not excluded, but blanket treatment of all cerebral embolic events with the same drug is likely to be ineffective and different drugs may be needed for different plaques.

Posters

Vaginal *versus* abdominal ultrasound for obtaining uterine artery Doppler flow velocity waveforms, by C. Steer, B. Rizk, S. L. Tan, B. Mason and S. Campbell
The story of Lesley, by P. Chudleigh
Contractions in the antenatal period after uterine artery flow velocity waveforms, by S. Bower, S. Vyas and S. Campbell
Granulomatous orchitis: an unusual cause of a testicular mass—a review of intratesticular mass lesions, by S. J. Gwyther
An echocardiographic study of giant-breed dogs with atrial fibrillation, by S. E. Brownlie
Prediction of re-bleeding from peptic ulcers using an endoscopic Doppler ultrasound detector, by D. Beckly and M. P. Casebow
Can computer-assisted impedance analysis (CAIA) assist in the identification of "at risk" femoro-distal grafts? by M. G.. Wyatt, R. M. Muir, W. G. Tennant, D. J. Scott, W. D. Jeans, R. Skidmore and M. Horrocks
Confusing appearances on breast ultrasound caused by fine needle aspiration, by W. E. Svensson, B. Al-Murrani, M. Blaszcyzyk, D. O. Cosgrove, A. Hounsom, A. Jones, T. J. Powles, H. D. Sinnett, E. Tohno and E. Vagios
Ultrasonic detection of a retroperitoneal haematoma causing duodenal obstruction following ureterolithotomy, by C. K. Frazer, D. A. Ritchie, A. D. Taylor and D. W. Newling
Development of a low cost portable Doppler flow phantom, by D. K. Nassiri and K. Fiaschi
Speckle reduction of Doppler waveforms by image processing, by P. R. Hoskins and T. Loupas
Transvaginal ultrasonographic assessment of intrauterine contraceptive devices, by J. H. Parsons and J. A. McEwan
The Doppler appearance of post biopsy arteriovenous fistulae in renal transplants, by D. L. Cochlin
Doppler investigation of the umbilical, renal and middle cerebral arteries in red cell iso-immunized fetuses, by S. Vyas, S. Bower, S. Campbell and K. Nicolaides
Maternal abdominal pressure alters fetal cerebral blood flow, by S. Bower, S. Vyas, S. Campbell and K. Nicolaides
Endoscopic ultrasound appearances of the stomach wall in portal hypertension, by D. MacVicar, S. Saverymuttu, A. Grammatopolous and A. E. A. Joseph
Real time cranial ultrasound in the evaluation of extra-axial collections in infancy, by C. I. Rothwell and T. Jaspan
Screening for aortic aneurysms—is frequent follow-up necessary? by W. G. Tennant, M. G. Wyatt, J. Hayward, D. J. A. Scott, H. Andrews and M. Horrocks
The natural history of acquired cystic disease of the kidney in dialysis and transplant patients, by P. L. Allan, S. R. Wild, D. A. S. Jenkins, A. Notghi, J. L. Anderton and R. Whinney
Vaginal ultrasonography—its value and limitations in the diagnosis of gynaecological pathologies, by N. Amso, L. Irvine, G. Buckland and R. W. Shaw
Doppler studies of renal dialysis fistulae utilizing colour flow mapping, by D. L. Cochlin
Ultrasonic appearance of non-neoplastic diseases of the bowel, by K. T. Khaw, L. J. Yeoman, S. H. Saverymuttu, M. G. Cook and A. E. A. Joseph
The sensitivity and specificity of ultrasound in the diagnosis of early pregnancy failure, by A. F. Riddle, V. Sharma, S. L. Tan, C. Steer, B. A. Mason and S. Campbell
Duplex sonography in splenomegaly, by L. J. Jarvis, P. G. Cook, C. M. James, M. Rose, A. G. Prentice and P. A. Dubbins
Follow-up of recurrent bladder tumours by transrectal and abdominal ultrasound, by A. H. Davies, D. Cranston, T. Meagher and G. J. Fellows
Ultrasound assessment of tongue movement on induction of anaesthesia, by L. J. Abernethy, P. L. Allan and G. B. Drummond
The value of ultrasound cervical assessment in the prediction of premature delivery, by G. Mason and M. Maresh
The ascent of the fetal spinal cord—an ultrasonographic–pathological correlative study, by P. Twining and J. Zuccollo
The sonographic appearances of four more unusual cases of Achilles tendon disease, by W. W. Gibbon and H. Mamtora
Automatic intermittent Doppler recording of Blood velocity in femorodistal bypass grafts by A. J. Thrush, N. Dahnoun and D. H. Evans
Computer-based system for feedback of obstetric ultrasound data and evaluation of ultrasonic measurement charts, by J. A. Evans, M. I. Plumb, J. K. Watters, B. Mostyn and P. Vinall
Ultrasonic endoscope based on a low cost personal computer, by M. Clarke, D. Simpson, D. Rutt and N. Browse

Vaginal *versus* abdominal ultrasound for obtaining uterine artery Doppler flow velocity waveforms

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It has been suggested that a potential cause of female infertility is decreased uterine artery perfusion. This has been postulated by quantifying changes in the flow velocity waveforms (FVW) obtained from the uterine arteries in patients who achieved a pregnancy as a result of *in vitro* fertilization and embryo transfer as compared with those who were unsuccessful in four or more attempts. Historically, these pulsed Doppler waveforms have been obtained from transabdominal transvesical ultrasound. However, varying the volume of urine in the bladder alters the angle of insonation between an abdominal transducer and the uterine arteries. Varying the angle of uterine retroversion may also alter the impedance to venous return. Using a Vingmed colour Doppler we have compared in 20 patients uterine artery FVWs obtained with a full bladder transabdominally transvescially using a 3 MHz transducer with those obtained transvaginally using a 7.5 MHz transducer. The vaginal FVWs were recorded with both a full and an empty bladder. The results were as follows: (1) FVWs obtained abdominally have a consistently higher pulsatility index than those obtained vaginally. (2) The FVWs obtained transvaginally were not significantly different whether the bladder was full or empty. We conclude that the increased diastolic frequency shifts obtained vaginally are as a consequence of a lower angle of insonation, and not due to bladder compression partially occluding venous return. This suggests that gynaecological Doppler studies of the uterine arteries should be performed in preference by the vaginal route.

The story of Lesley

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Once upon a time there lived a... Its main hobby was embedding. For about two and a half weeks no one knew it was there. Its secret was safe until a few days after the next period was due. Using... things looked much the same but with... It waited some weeks for its cerebral cortex to develop sufficiently and then thought "Well knock me down with a feather,... is without doubt the transducer of choice. Every D.G.H. should have one". Six weeks had passed since the L.M.P. As the embryo grew it played a game "test the operator"... Time passed and by 18 weeks the fetus could distinguish between... and a... The heart had... The spine was... right down to the flip-up of the... The intact... showed there was no... There was no... because... showed a single stomach bubble... and... were excluded because of the normal... The kidneys... could be easily identified and... excluded. It discovered it had... "Well of course these fancy tests are never 100%" a voice said. He looked down, "looks pretty 100% to me" he thought. Just in case he'd "got it wrong" he decided to call himself Lesley. Lesley was impressed to find out he appeared structurally normal only 10 min after he'd got onto the couch. He was also pleased that his Dad had been watching all the way through. At 37 weeks he was still breech so got sent off for a weight estimation. "This'll fox them" he thought as he looked at the measurements. "Are they going to use Campbell, Shepard, Hadlock or toss a coin. Strikes me they need to do a multi-centre study into fetal weight estimations. The BMUS working party was right. Nothing for it but to await delivery." And with that he... and rolled over.

Contractions in the antenatal period after uterine artery flow velocity waveforms

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Uterine contractions during labour are known to alter uterine artery flow velocity waveforms. The uterus also contracts prior to the onset of labour and the aim of this study was to investigate the effect of these contractions on abnormal uterine artery flow velocity waveforms. Eight women who were found at routine screening to have abnormal uterine artery flow velocity waveforms were recruited. With the women in the semi-recumbent position, colour-flow imaging was used to identify the uterine artery and external tocography was performed simultaneously. The pulsatility index of uterine artery flow velocity waveforms was measured at intervals of 2–7 min and was found to increase when contractions were recorded on the tocograph. Three women were started on the calcium-antagonist Nifedipine and were found to have fewer contractions after 1 week of treatment. Contractions in the antenatal period alter uterine artery flow velocity waveforms and may therefore intermittently reduce uterine perfusion. These preliminary results indicate that the tocolytic effect of Nifedipine may be of benefit in cases with diminished uterine perfusion.

Granulomatous orchitis: an unusual cause of a testicular mass—a review of intratesticular mass lesions

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A 55-year-old West Indian man presented with right sided loin and testicular pain. On examination an enlarged, tender, hard, right testis and firm, mobile occipital lymph node were detected. Testicular ultrasound examination demonstrated multiple, well defined, bilateral, hypoechoic lesions. Over the next month the testicular lesions increased in both size and number. The occipital lymph node was excised and the histology revealed Kaposi's sarcoma. The patient was human immunodeficiency virus (HIV) antibody negative and there were no risk factors to render him immunocompromised. Radical unilateral orchidectomy was performed. The histology revealed granulomatous orchitis, a rare benign condition, only about 160 cases having been reported. It is usually misdiagnosed clinically and ultrasonically as a testicular tumour or infection, the true diagnosis only being made histologically. This patient was initially thought to have a testicular tumour. The bilateral, multifocal pattern suggested metastases or lymphoma, and having had Kaposi's sarcoma recently diagnosed strengthened this argument. Tuberculosis or syphilis were possible alternative diagnoses, but less likely from the history and serological investigations. The characteristic ultrasonic features of primary testicular tumours, metastases, chronic inflammatory and granulomatous conditions causing intratesticular mass lesions are briefly described. The paper illustrates a rather unusual cause of a testicular mass and discusses the differential diagnosis. It also emphasizes that the definitive diagnosis of intratesticular lesions can only be made histologically.

An echocardiographic study of giant-breed dogs with atrial fibrillation

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A trial fibrillation is a common arrhythmia in giant breed dogs. Cases presented to veterinary surgeons are usually in left sided heart failure due to dilated cardiomyopathy, with clinical signs of dyspnoea, coughing and collapsing episodes. However, a survey carried out by the author in one breed (Irish Wolfhounds) has shown that 11% of normal dogs and bitches have asymptomatic atrial fibrillation, and the prognostic significance of this finding is uncertain. Ultrasound examination (2-D and M-mode) was carried out in three groups of giant breed dogs to assess basic left-sided heart measurements. The groups were (1) normal dogs, (2) asymptomatic dogs with atrial fibrillation and (3) symptomatic dogs with atrial fibrillation. Measurements were obtained using a Kontron Sigma SC sectoscanner and a 5 MHz transducer from a right parasternal position. Left ventricular systolic and diastolic internal diameter, left ventricular free wall thickness, in systole and diastole, and septal thickness were measured from a short axis view at the level of the chordae tendinae. Fractional shortening was then calculated. The diameter of the aortic root was measured from a short axis view at the level of the aortic valve, and maximum left atrial diameter was measured from a long axis view. The results from the symptomatic group show a significant increase in measurements of left atrial size, left ventricular systolic and diastolic internal diameter and a decrease in fractional shortening, compared with the normal, as is to be expected in dilated cardiomyopathy. These measurements in the asymptomatic group are similarly altered, though not to such a marked degree, confirming that these dogs are early cardiomyopathy cases and should be given a guarded prognosis.

Prediction of re-bleeding from peptic ulcers using an endoscopic Doppler ultrasound detector

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Between 10% and 30% of patients with bleeding peptic ulcers suffer a re-bleed that is either fatal or serious enough to require immediate surgery. The visible appearance of the ulcer allows some prediction of its chances of re-bleeding but is not accurate enough to influence the decision about surgery. A small Doppler ultrasound probe capable of being passed down the biopsy channel of a gastro-scope was therefore developed some years ago in order to improve the prediction of re-bleeding, based on the presence or absence of a pulsatile Doppler signal from the base of the ulcer. This is now used routinely in clinical decisions concerning the patients' management. The current results of a continuing endoscopic assessment of the prediction of re-bleeding peptic ulcers is presented.

Can computer-assisted impedance analysis (CAIA) assist in the identification of "at risk" femoro-distal grafts?

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Graft surveillance following femoro-distal bypass is time consuming and expensive, but the detection and correction of graft or run-off stenoses prior to graft failure can improve both graft patency and limb survival rates. We have devised a non-invasive method of measuring limb impedance in an attempt to identify those grafts likely to fail post-operatively. Forty patients with functioning non-reversed femoro-distal vein grafts were studied (M:F = 30:10, median age 73 years). For each patient groin and lower graft Doppler signals were obtained using a standard 10 MHz pencil probe and stored on a portable 2100 Toshiba computer as the "input waveforms". Thigh and calf pulse volume recordings (PVR) were stored as the "output waveforms". Fast Fourier transform analysis was performed on the paired Doppler/PVR waveforms and an indirect impedance score derived for the thigh and calf respectively (arbitrary units). Each patient underwent intra-arterial digital subtraction arteriography (DSA) and the grafts defined as "at risk" or controls dependent upon the presence or absence of graft or run-off stenoses.

	Controls	"At risk"
Patient number	22	18
Thigh impedance	0.33 + (0.28–0.37)	0.58 + (0.43–0.72)[a]
Calf impedance	0.34 + (0.32–0.36)	0.54 + (0.48–0.60)[a]

(Mean + 95% confidence interval: [a]$p < 0.001$ Mann–Whitney U test.)

A thigh or calf impedance value of > 0.45 was able to predict graft or run-off stenoses in 100% cases with a reproducibility of 98%. Computer-assisted impedance analysis (CAIA) is new and may have a role in the identification of "at risk" grafts before they fail.

Confusing appearances on breast ultrasound caused by fine needle aspiration

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Fine needle aspiration is sometimes suspected as the cause of abnormal appearances on breast ultrasound. Haemorrhage at the biopsy site may produce suspicious features that mimic malignancy. This paper reports work in progress on patients with breast masses who have an ultrasound scan prior to fine needle aspiration biopsy (FNAB) by the referring clinician. Immediately following the needling, the scan was repeated and any change in the appearances that would have altered the diagnostic category was noted. In those cases where a change was shown, follow-up scans were performed over subsequent weeks (unless the patient was referred for surgery) to assess the time needed for resolution of the needle-induced changes. In the 15 cases studied so far, over 25% showed a change in appearance after FNAB and in three cases the change would have raised the suspicion of malignancy when the initial examination had been normal or showed a benign lesion. Previous observations have suggested that these changes can persist for up to 3 months; this study will show in what proportion of cases this is true. Our initial observations indicate that FNAB causes a significant increase in confusing ultrasound appearances. The practice of needling suspicious regions in the breast prior to scanning increases interpretative difficulty by producing misleading ultrasound features that suggest malignancy.

Ultrasonic detection of a retroperitoneal haematoma causing duodenal obstruction following ureterolithotomy

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A 51-year-old male had an open ureterolithotomy for an impacted calculus in the distal right ureter but the operation was technically difficult owing to scarring and adhesions from previous ureteric surgery. He was discharged after 10 days but readmitted 4 days later with a history of bile stained vomiting and upper abdominal distension. Ultrasound revealed a large inhomogeneous hypoechoic mass in the right upper abdomen lying anterior to the inferior vena cava and right kidney and extending inferiorly into the right paracolic gutter. Medially the mass surrounded and compressed the second part of duodenum with a characteristic "converging walls" sign, causing obstruction. These findings suggested the mass was located in the right anterior pararenal space of the retroperitoneum, and in view of the recent surgery a confident diagnosis of retroperitoneal haematoma was made. This was confirmed at laparotomy which demonstrated extension of the haematoma into the right infra-colic compartment to the site of the previous surgery. Removal of the haematoma was not possible and a gastroenterostomy was performed. These ultrasound appearances are not specific and similar findings have been noted with intramural haematomas, especially when they occur with retroperitoneal bleeding which commonly accompanies blunt epigastric trauma. However, isolated intramural haematoma can occur and usually presents as a smaller more circumscribed mass. Although inflammatory and neoplastic causes could also be considered, the ultrasonic appearances together with the clinical history were highly suggestive of the diagnosis.

Development of a low cost portable Doppler flow phantom

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Despite the widespread acceptance and use of Doppler ultrasound in clinical practice, and rapid developments in this field, there is not yet a consensus agreement on the methods of assessing Doppler ultrasound performance. A Doppler flow phantom has been designed and developed to meet the ultimate objective of producing a simple, reliable, and versatile portable phantom for use in both rigorous acceptance tests and quick routine checks. This system has been designed to take account of the wide variation in commercially available Doppler probes and to reflect the need for clinically relevant performance measurements. Steady flow has been produced by a dual reservoir system, with hydrostatic pressure driving the blood-mimicking fluid, through three parallel tubes of different diameters, and at angles of 60° to the vertical. In addition, a fourth tube at 30° to the vertical has been incorporated. A pump, independent from the measurement window, has been used to return the fluid to the upper reservoir, thereby completing the flow circuit. The requirement of compactness has been satisfied by limiting the total fluid capacity to 2 l. Also, a probe holder has been designed which allows precise movement in a horizontal plane. An adjustable height upper reservoir has provided the means of checking the accuracy of velocity and flow measurements. The phantom has been used successfully to test sensitivity, depth, range and registration accuracy, and soft-tissue-mimicking material, situated between the probe and flow region, has provided measurements under different signal-to-noise conditions. A pulsatile flow generator, a mechanical device driven by a motor, has been incorporated to simulate more closely physiological behaviour. This paper will discuss the use of starch, Sephadex and silicon solutions as blood-mimicking fluids.

Speckle reduction of Doppler waveforms by image processing

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Recently there has been interest in the production of Doppler spectra using spectral estimation techniques other than the Fourier transform (FT), in order to attempt to reduce speckle and increase resolution. However, all of the currently available commercial spectrum analysers use FT spectrum analysis. An alternative approach to speckle reduction is the use of filtering applied to the conventional FT spectrum. In this study three filters are compared in terms of the balance achieved between noise reduction and edge preservation in different parts of the image. The three filters are the double window modified trimmed mean (DWMTM) filter, Lee's filter and directional filter. A number of local image measures for the control of the degree of filtering produced by Lee's filter and the directional filter were considered. These filters were applied to a variety of regular waveforms obtained from a physiological flow phantom. Ensemble averaging of 168 waveforms was performed, enabling bias and noise reduction produced by filtering to be examined. The filter with the best performance is the directional filter. The local image measure used to control the aggressiveness of this directional filter was chosen as the ratio of an edge detection parameter $R(d)$ over a slope parameter $\mathrm{SL}(d)$ for the direction d.

Transvaginal ultrasonographic assessment of intrauterine contraceptive devices

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A very significant number of women who have intrauterine contraceptive devices (IUCD) inserted have them removed within the first year because of problems attributed to the device. These problems include pelvic pain, menstrual disturbance, intermenstrual bleeding, infection and pregnancy. Malposition of the device may be a contributory factor but investigation of such a correlation has not been feasible using hysterosalpingography and hysteroscopy. Transabdominal ultrasonography through the full bladder does not give adequate information. The uterus may now be visualized clearly with minimal discomfort to the patient with transvaginal ultrasonography. It is now possible to define clearly the uterine cavity and the exact position of the stem of the device and its arms. To investigate the relationship between the position of IUCDs within the endometrial cavity and gynaecological symptoms we recruited 41 patients—23 who wished to have a device inserted (Group A) and 18 who had been wearing one for at least 12 months (Group B). Group A patients were scanned within 3 days of insertion of a device and Group B on entry to the study. Both groups were scanned on a second occasion 3 months later. All scanning was performed with a 7 MHz transvaginal sector scanner (Bruel and Kjaer). Detailed symptom charts were kept by the patients throughout the study. In six patients scanning revealed the device to be in a grossly abnormal position (two embedded, one rotated, three descended). The correlation between abnormal position and symptoms was poor (sensitivity 60%, specificity 48%). It is important that the significance of this high number of apparently abnormal findings is evaluated as appropriate management strategies must now be developed.

The Doppler appearance of post-biopsy arteriovenous fistulae in renal transplants

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Arteriovenous fistulae are common following biopsy of transplanted kidneys occurring in up to 25% of cases. The majority are short lived, spontaneously closing after about 48 h. A minority, however, persist and enlarge until they compromise renal function. An understanding of the Doppler findings is important in those cases where function is compromised, and also in earlier cases, where the appearances may confuse the sonographer. This presentation is based on 11 cases, five proven by angiography, these being the ones that became symptomatic, the other six showing spontaneous closure. The appearance in all the early cases comprised high venous flow, with far greater pulsatility than in a normal renal vein. The arterial flow appeared normal, and only in a minority of cases was a high velocity jet at the actual fistula demonstrated. The fistulae that enlarged showed large venous spaces, with pulsatile flow in some only. One in addition showed upper pole hydronephrosis from an aneurysmal vein at the hilum, fed by an upper pole AV fistula, which obstructed the upper pole infundibulae. One AV fistula was subsequently inadvertently biopsied at a repeat biopsy, and well demonstrated on the histological slide. Colour flow mapping became available towards the end of this study, and this enables more precise information to be obtained, the feeding artery being more readily identified, and the fistula being more easily visible on the preliminary examination of the kidney. It seems likely that colour flow will make Doppler ultrasound more sensitive in the detection of AV fistulae, though as yet our numbers are too small to prove this. We conclude that a knowledge of the appearance of AV renal fistulae on Doppler ultrasound is important to anyone studying transplanted kidneys. Fistulae when found should be followed by serial examinations to ensure closure. Fistulae shown to be enlarging should proceed to angiography and embolization if technically possible.

Doppler investigation of the umbilical, renal and middle cerebral arteries in red cell iso-immunized fetuses

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In red cell iso-immunization there are varying degrees of haemolysis and anaemia. The fetus compensates for this reduction in oxygen-carrying capacity by haemodynamic adjustments, and Doppler studies have demonstrated an increase in aortic mean blood velocity with anaemia. The aim of this study was to investigate the relationship of fetal anaemia and Doppler findings in the fetal umbilical, renal and middle cerebral arteries, since it has been suggested that the increase in aortic mean blood velocity may be secondary to a reduction in impedence to flow in the peripheral circulation. Twenty-four previously untransfused fetuses had Doppler investigations of the umbilical, middle cerebral and renal arteries immediately before cordocentesis. The pulsatility index was significantly lower than the normal mean for gestation in the umbilical and middle cerebral arteries. This reduction in impedence to flow, however, was not related to the degree of anaemia. The middle cerebral artery mean blood velocity was significantly higher than the normal mean for gestation, and there was a significant linear correlation between the increase in middle cerebral artery mean blood velocity and anaemia. Although there was a significant relationship between the fall in impedence to flow and mean blood velocity in the middle cerebral artery, this association did not completely explain the increase in mean blood velocity. Thus, although the reduction in peripheral impedence to flow may be responsible for the increase in mean blood velocity, other factors, such as blood viscosity and cardiac contractility, may also play a role.

Maternal abdominal pressure alters fetal cerebral blood flow

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Colour flow imaging was used to identify the fetal aorta, middle cerebral and internal carotid arteries for subsequent pulsed Doppler studies in 45 appropriate for gestational age fetuses. The pressure applied to the fetal head by the ultrasound transducer was measured by an open-ended water filled manometer. Significant positive correlations were found between an increase in the pressure applied and an increase in the pulsatility index of flow velocity waveforms from the fetal intra-cranial vessels, but not the aorta. These relationships differed with gestational age. The pressure exerted during routine measurement of the fetal biparietal diameter was also measured, and was found to be similar to that which causes alterations in fetal intra-cranial haemodynamics. It is proposed that fetal head compression leads to an increase in intra-cranial pressure and thus an increase in impedence to flow. These changes are not seen in the fetal aorta, which unlike the brain is not enclosed in a rigid "box". Doppler examination of the fetal intra-cranial vessels is providing information on the head-sparing effect in hypoxaemic small for gestational age fetuses. These findings indicate that minimal transducer pressure should be applied during Doppler examinations if a high false negative rate is to be avoided.

Endoscopic ultrasound appearances of the stomach wall in portal hypertension

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The thickness of the stomach wall on ultrasound has recently been shown to be increased in patients with hepatic cirrhosis and portal hypertension. The histological abnormality underlying this observation is still uncertain. Striking changes in the gastric vasculature, with dilated, tortuous submucosal veins have been demonstrated in pathological specimens from gastric resection or post mortem examinations on patients with portal hypertension. These changes have been termed "congestive gastropathy" and it seems likely that they are responsible for the gastric thickening seen on abdominal ultrasound. To test this hypothesis, we have undertaken endoscopic ultrasound of the gastric wall in patients with portal hypertension. This technique allows more accurate visualization of the submucosal layers. The findings will be demonstrated and their pathological and practical significance will be discussed.

Real time cranial ultrasound in the evaluation of extra-axial collections in infancy

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Twenty-four patients (age 3 weeks to 8 months) with suspected extra-axial collections were examined on an Acuson 128 scanner. The clinical indications were direct accidental trauma (10) suspected non-accidental injury (six), meningitis (three), rapidly increasing head circumference (four) and deterioration following tapping of known subdural collections (one). Scanning was performed through the anterior fontanelle and via the trans-squamosal approach in all cases. In most cases a 5 or 7 MHz linear array probe was employed to assess the near field over the cerebral convexities. All examinations were performed without sedation. Correlative CT scans were performed in four cases, and MRI scans in two. Findings were confirmed surgically in two patients and at post mortem in a further two cases. No other imaging modality was employed in 14 cases, the diagnosis being verified by tapping of subdural collections in seven cases. The presence of subclinical small collections or absence of a collection demonstrated by ultrasound was confirmed by follow up ultrasonography in seven patients, coupled with clinical findings of lack of increase in the head circumference and general well being of the child. In total 17 patients were shown to have extra-axial collections, nine with subdural haematomas, one extradural haematoma and seven cases in which CSF filled extracranial collections were felt to be consistent with communicating hydrocephalus. The anterior fontanelle was superior for the demonstration of fine anatomical detail and assessment of any associated parenchymal damage. Differentiation of subdural from subarachnoid collections could be made with the linear array probes via this route. Transquamosal scanning was optimal for the assessment of more laterally situated collections. We conclude that ultrasound is a simple non-invasive and accurate technique for the demonstration of extra-axial collections in neonates and infants. The technique has now become our primary investigation in the evaluation of suspected extra-axial collections in infants.

Screening for aortic aneurysms—is frequent follow-up necessary?

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Screening for aortic aneurysm is now being undertaken in many centres. Follow-up intervals for those without aortic aneurysm, but with aortic dilation have not been defined. We have studied 209 male patients over two years to assess the change in aortic diameter, and report the influence of hypertension on aortic diameter with time. The original study group comprised 209 male patients in the following groups: Group 1, 88 normotensive male patients; Group 2, 87 male patients with well-controlled hypertenison; Group 3, 34 male patients with severe hypertension requiring hospital admission for control. There were no significant differences in height or weight between the three groups, but Group 3 was significantly younger than the other two groups, ($p < 0.001$ in both cases, Mann Whitney U-test). The aortic diameter was significantly greater in Group 3 than in Group 1 ($p < 0.002$), and Group 2 ($p < 0.001$). Four patients had an aortic diameter over 4 cm and were offered surgery. One hundred and thirty two patients attended for rescreening, and the results are as follows:

	Mean aortic diameter (mm)		
	1987	1989	Change
Group 1 ($n = 60$)	19.23 ± 0.37	20.12 ± 0.40	0.88 ± 0.38
Group 2 ($n = 43$)	18.86 ± 0.56	19.72 ± 0.35	0.91 ± 0.57
Group 3 ($n = 29$)	22.03 ± 1.31	22.86 ± 1.75	0.83 ± 0.85

The change in diameter was not significant within or between groups (Mann–Whitney U test). In only one of the 45 patients with an original aortic diameter greater than 20 mm had the diameter changed over 4 mm (normotensive patient, changed from 20 to 27 mm). This study suggests that frequent follow-up examinations of patients screened for aortic aneurysm may be unnecessary. Severe hypertension appears to have no influence on this finding.

The natural history of acquired cystic disease of the kidney in dialysis and transplant patients

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Acquired cystic disease of the kidney (ACDK) is a recognized association of dialysis therapy and may be complicated by haemorrhage and neoplastic change. We have previously reported (1985) on the prevalence of ACDK in our dialysis population and in a group of transplant patients. Our results showed a close correlation with duration of dialysis and that transplant patients were less severely affected than dialysis patients. We have re-examined the surviving patients from this original group. Thirty-one died, two have moved, 19 have received a transplant and 40 of the 48 patients remaining on dialysis were available for follow-up. Changes were graded 0–4 as previously and for this dialysis group showed a marked progression over the interval:

	1985	1989
Grade 0	10 (25%)	2 (5%)
Grade 1	10 (25%)	8 (20%)
Grade 2	5 (12.5%)	4 (10%)
Grade 3	6 (15%)	12 (30%)
Grade 4	9 (22.5%)	14 (35%) $p < 0.0001$
Solid lesions	1 (2.5%)	4 (10%)

The results for those patients from the initial study who have been transplanted during the interval and for those patients who have had a continually functioning transplant are currently being collated. Preliminary data suggest that the changes of ACDK in these patients are less marked than in the dialysis group, confirming our original suggestion that transplantation has a retarding influence on the development of ACDK.

Vaginal ultrasonography—its value and limitations in the diagnosis of gynaecological pathologies

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Vaginal ultrasonography has become an established tool for monitoring follicular growth, oocyte retrieval and the diagnosis of early intra-uterine or extra-uterine) pregnancy. It obviates the need for a full bladder with all its inconvenience and allows better visualization of the structures being examined because of the proximity and higher frequency of the ultrasound crystal used. The aim of this study is to evaluate the diagnostic role of vaginal ultrasound for the diagnosis of selected gynaecological pathologies in comparison with abdominal scanning and the operative findings at laparoscopy, laparotomy and D&C. Forty women have so far been included in this study. Vaginal and abdominal scanning was carried out within one week of their operation using a Diasonics machine equipped with a 7.5 MHz transvaginal probe and a 3.5 MHz general purpose probe. The pathologies included uterine fibroids, ovarian cysts, suspected ectopic pregnancies, dysfunctional uterine bleeding and perimenopausal bleeding. All vaginal scans were performed by one operator who was unaware of the abdominal scan findings. The pelvis was examined in the sagittal then coronal planes to determine cervical-uterine position and abnormalities and then the appearance of the ovaries, adnexa and the pouch of Douglas. All pathologies except one were seen on vaginal scanning. Uterine fibroids were easily seen vaginally except when the uterine size exceeded the depth of field. Abdominal scanning was superior in this respect. Similarly, ovarian and adnexal masses were more clearly distinguishable vaginally particularly in obese patients. The pathology that was not seen vaginally was a tubo-ovarian mass displaced abdominally by a gravid uterus. In conclusion, vaginal ultrasonography gives superior imaging quality when the pathology is confined to the pelvis and also in obese patients. However, it cannot totally replace abdominal scanning.

Doppler studies of renal dialysis fistulae utilizing colour flow mapping

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Renal dialysis fistulae may malfunction in several ways. They may provide inadequate dialysis owing to reduced flow; ischaemia of the fingers may occur owing to excessive flow and they may become thrombosed or pseudo-aneurysms may develop. Traditionally, these problems have been investigated by angiography of the venous or arterial side of the fistula, or both. While giving good anatomical information, such studies only give a wide estimation of flow. Doppler studies with colour flow mapping can give equivalent anatomical information in a non-invasive test and give far superior measurement of flow in the arteries and veins comprising the fistula complex. We have studied 20 normally functioning dialysis fistulae and six fistulae with complications, by colour flow and spectral Doppler. We have demonstrated the anatomy sufficiently well to enable useful flow measurements to be obtained by spectral Doppler. Volume flow can be estimated in the radial artery and veins comprising the fistula. An arterial flow lower than the venous flow indicates steal from the hand with reversed flow in the radial artery distal to the fistula. This can be confirmed by studying the radial artery at the thenar eminence. Direction of flow and velocity may be measured, though the diameter of this artery is too small to enable accurate volume flow to be calculated. The volume flow in the ulnar artery in the lower forearm can be measured. Subtracting arterial flow in radial and ulnar arteries from the venous flow in the fistula (ignoring flow in other veins) gives a crude but valuable estimate of the blood flow to the hand. Venous thrombosis is readily demonstrated, and haemotomas and pseudo-aneurysms are readily detected. We conclude that colour flow and spectral Doppler examinations are now the investigations of choice in complications of dialysis fistulae. They may also be used as a research tool for measuring changes in flow in fistulae over time, or the effect of drugs such as synthetic erythropoietin on flow.

Ultrasonic appearances of non-neoplastic diseases of the bowel

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Ultrasound is a useful adjunct in the investigation and follow-up of patients with bowel pathology. Abnormality can be reliably detected in a wide range of conditions. One hundred and seventeen ultrasound scans were performed in 90 patients with suspected bowel pathology. In all 90 patients the diagnoses were proven by histology, radiology or other laboratory investigations and are summarized below.

Diagnosis	No.	Diagnosis	No.
Crohns	46	Colitides:	
Ulcerative colitis	12	Ischaemic	3
Tuberculosis	4	Salmonella	6
Amoebiasis	2	Pseudomembranous	3
Diverticulitis	10	Cytomegalovirus	2
Infarction	2		

The abnormality most commonly recognized was thickening of the bowel wall. Two different patterns of abnormality with different degrees of wall thickening could be recognized corresponding to Crohn's disease and ulcerative colitis. The appearance in other conditions usually corresponded to either the Crohn's type or ulcerative colitic-type pattern, and could be related to the underlying pathological changes. In addition, two other appearances were recognized which were "thumb-printing" in ischaemic colitis and a "concertina" pattern in diverticular disease. Complications such as small bowel obstruction and collections were demonstrated. The patterns of abnormality and ultrasonic findings in these patients are described with relation to the pathology and examples shown.

The sensitivity and specificity of ultrasound in the diagnosis of early pregnancy failure

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One hundred and fifty four IVF pregnancies were monitored by weekly transabdominal ultrasound starting 3 weeks after embryo transfer until the end of the first trimester. Eighty-two singleton, 28 twin and one triplet pregnancy continued to viability while 43 pregnancies failed (14 ectopic, 29 intrauterine). Normal ranges for the crown rump length and gestational sac volume were produced. Deviation from normal of the gestational sac volume on one occasion had a low specificity and sensitivity for diagnosing pregnancy failure. If the gestation sac was not identified by week 6, pregnancy failure was common. The presence of fetal pole and fetal heart activity by week 7 had the highest specificity and sensitivity for predicting progress to viability ($>93\%$). Conversely, the absence of fetal heart by week 7 was diagnostic of pregnancy failure. All ectopic pregnancies were suspected but not positively identified, while all multiple pregnancies were correctly diagnosed by week 7. We conclude that with transabdominal ultrasound scanning a single scan at week 7 would have the highest sensitivity and specificity for diagnosing failed pregnancy.

Duplex sonography in splenomegaly

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The aetiology of splenomegaly is seldom clear from either clinical or imaging assessment of the spleen. In the majority of cases sonographic assessment of the spleen produces a homogeneous enlargement of variable echodensity, but with very poor correlation with pathology. A study has been undertaken to assess the Doppler characteristics of the splenic artery in splenomegaly, excluding cases of portal hypertension in an attempt to provide further diagnostic information. Duplex assessment of 18 normal subjects and 10 patients with splenomegaly due to five different causes was undertaken. Analysis of waveform, peak frequency and pulsatility index were compared and failed to demonstrate any significant change. In the normal subject there is a broad systolic spectrum related to the tortuosity of the splenic artery, with persistence of forward flow throughout diastole, a reflection of the low peripheral resistance of the spleen. In splenomegaly the broad systolic spectrum is unchanged, since vessel tortuosity persists. Pathological and physiological assessment of the spleen in splenomegaly shows that a low resistance circulation persists, explaining a maintenance of the diastolic flow pattern in splenomegaly. Increased blood flow to the spleen in splenomegaly occurs either as a result of an increase in vessel diameter or an increase in flow velocity, or a variable combination of the two which does not seem to be governed by specific pathology. An increase in peak frequency in some cases reflected some increase in flow velocity but provided no useful correlation. Analysis of the pulsatility index supported the above findings without adding further information.

Follow-up of recurrent bladder tumours by transrectal and abdominal ultrasound

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Cystoscopy is the routine method used for follow-up of recurrent bladder tumours this forms a major part of the urological workload. A reliable less invasive method would have numerous advantages. The role of ultrasound in the clinical setting was investigated and compared with cystoscopy. One hundred and twenty five patients (100 males, 25 females) of mean age 62 years (41–83) with previously known bladder tumours were examined initially using the Bruel & Kjaer 1846 ultrasound machine using the 4 MHz abdominal probe and the 7 MHz transrectal probe and urine was sent for cytology the week before the cystoscopy, which was then performed under general anaesthetic. Sixty (48%) patients had recurrent tumour. 77% were detected by transrectal ultrasound, 82% by abdominal ultrasound and 90% in combination. Cytology detected 62% of tumours and the sensitivity of combination ultrasound with cytology was 93%. Ten (8%) patients were said to have had an inadequate ultrasound examination and cystoscopic examination would have been recommended. If a correction is made for this, combination ultrasound detected 97% of patients with recurrence. The tumours missed were 2 mm in diameter or less. The false positive rate was 2%. All except one elderly woman stated a preference for the ultrasound technique, in comparison to having a check cystoscopy. By the time of the meeting we hope to be able to present data on at least 200 patients. This series demonstrates that combination ultrasound is a sensitive method of following up patients with bladder tumours. We feel that the above results allows us to modify our mode of follow up of bladder tumours. It is a technique that can be used either by the radiologist or urologist.

Ultrasound assessment of tongue movement on induction of anaesthesia

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Maintenance of patent airway is a common problem in general anaesthesia. Airway obstruction is often attributed to "falling back" of the tongue, resulting in occlusion of the oropharynx. To assess the degree of tongue movement during the induction of anaesthesia we used realtime ultrasound to study women about to undergo minor gynaecological procedures, obtaining satisfactory data in 11 patients. The patient relaxed with her head in a natural position. An image of a sagittal midline section of the tongue was obtained with a 3.5 MHz sector transducer (Siemens Sonoline SX) placed below the chin. The transducer was clamped in the position which gave the best image and a video recording obtained as anaesthesia was induced, continuing until at least 1 min after loss of consciousness. Time of loss of consciousness and episodes of airway obstruction were recorded. Photographs of individual frames were taken from the video recordings and coded in random sequence. The outlines of the tongue surface were traced and measurements were made along the radius of the sector, the anterior, middle and posterior points of the tongue surface, although the hyoid bone occasionally obscured the posterior segment. Movements observed were small and there was no consistent direction of movement. There was no relationship between movement and the occurence of clinically apparent airway obstruction. The probability of any movement of more than 8 mm was less than 28% (95% confidence limits, binomial distribution). Ultrasound has proved a practical means of investigating tongue movement and we conclude that tongue movement on induction of anaesthesia is small and inconsistent.

The value of ultrasound cervical assessment in the prediction of premature delivery

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A blind prospective study was designed to investigate the true value of ultrasound cervical measurements in the prediction of women delivering prematurely. Three groups of women were studied: 122 with a history of at least one delivery between 16 and 35 weeks gestation, 20 with a clinically increased risk of premature delivery and 30 controls were investigated by serial ultrasound cervical assessments. In total, 1327 such assessments were performed usually at two-weekly intervals using a GL Z series sector scanner with a 3.5 MHz probe. At each visit the cervical length and the diameters of the internal os, cervical canal and the external os were recorded. The position of the internal os was located at the presumed ultrasound equivalent of the histological internal os. Voided bladder volumes were recorded and cervical length adjusted accordingly. The results for the control patients demonstrate that the normal ultrasound cervical length, when adjusted for bladder volume, decreases throughout the second and third trimester. The internal and external os and cervical canal demonstrate a progressive dilatation which is maximal in the third trimester. The range of normal cervical length measurements are such, however, to be of no value in the prediction of premature delivery. Dilatation of the internal os, in particular, with protrusion of fetal membranes into the canal is the most reliable parameter. Nevertheless in half of the women considered to have genuine cervical incompetence in the index pregnancy, the internal os diameter was within the normal range at the assessment which preceded delivery. Increased success may have been achieved, however, if ultrasound assessments had been performed more frequently. In conclusion, although serial ultrasound cervical assessments are very reassuring to the "at risk" patient, they are of limited value in the prediction of premature delivery and single assessments are of no value in the diagnosis of cervical incompetence.

The ascent of the fetal spinal cord—an ultrasonographic–pathological correlative study

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In the embryo the spinal cord extends down to fill the entire spinal canal. During the first 24 weeks of pregnancy the tip of the spinal cord ascends to lie at the L3/4 level, so that the major part of cord ascent occurs in the first half of pregnancy. In the neonate, the tip of the cord lies at the L3 level and during childhood ascends to the adult position of L1/2 level. The ascent of the cord is predominantly produced by disproportionately more rapid growth of the vertebral column and this study set out to course the ascent of the cord from 14 weeks gestation onwards. Antenatal scans were carried out on 50 fetuses ranging from 16–40 weeks gestation in order to assess the lower level of the spinal cord. Scans of the spine were obtained in the sagittal and coronal planes through the midline with the fetus "spine up". In addition, post mortem ultrasound scans were carried out on 25 fetuses ranging in gestational age 14–38 weeks. Scans were obtained of the spine and the level of the cord assessed, using a water bath technique and also contact scanning. Pathological studies were then carried out and longitudinal cryomichrotome sections were taken in order to assess the level of the tip of the cord. The ultrasound appearances and cryomichrotome sections were compared and the level of the cord assessed for each gestational age. It was found that at 14 weeks gestation the tip of the cord extended down to the level of S2/3, by 18 weeks the cord had ascended to L5/S1 and that by 24 weeks the tip of the cord had reached L3/4 level.

The sonographic appearances of four more unusual cases of Achilles tendon disease

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The sonographic features of Achilles tendon tenosynovitis and chronic tendonitis are well recognized. The present poster demonstrates four more unusual cases of Achilles tendon disease. (1) Bilateral asymptomatic chronic Achilles tendonitis in a 33-year-old female with chronic renal failure and hypercalcaemia examined as part of a separate study into the possible association between hypercalcaemia and Achilles tendon disease. There was no history of steroid therapy, inflammatory arthropathy nor other additional predisposing factor to Achilles tendon disease. Sonographic appearances were unequivocally those of chronic tendonitis. (2) Symtomatic dense focus of calcification centrally within the Achilles tendon of a 71-year-old female with primary hyperparathyroidism. The patient had noticed increasing discomfort within her right Achilles tendon over the previous 2–3 weeks. There was no previous history of trauma nor any other Achilles tendon problem. Sonographic examination revealed a large intratendinous calcium deposit with marked surrounding tenosynovitis. Both cases (1) and (2) may give a pointer towards the possible pathogenesis of Achilles tendon rupture in renal disease. (3) Bilateral symptomatic osteochondritis of the Achilles tendon insertion into the os calcis (Sever's disease) in a 23-year-old footballer. Ultrasound was able to demonstrate fragmentation of the bony insertions later confirmed on plain radiography. It was also able to show localized thickening and echo-pattern changes consistent with chronic tendinitis within the distal tendo-Achilles with superimposed tenosynovitis in region of bony fragmentation. (4) Mild tenosynovitis of the left Achilles tendon following a fall from a ladder 4 weeks previously. It was noted at the time of examination that the 56-year-old male walked with an arthralgic gait. Sonographic examination of his tender forefoot revealed a healing fracture of his second metatarsal shaft which was confirmed by radiography. The tendo-Achilles changes were presumably secondary to the patient's altered gait. Ultrasound clearly demonstrated both fracture site and associated callus formation. The cases give evidence as to the diagnostic scope of high definition ultrasound in the diagnosis of Achilles tendon disease.

Automatic intermittent Doppler recording of blood velocity in femorodistal bypass grafts

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Many femorodistal grafts fail without indication within the first few days after surgery. A system for recording the Doppler signal from femorodistal grafts over the early post-operative period has been developed. A specially designed probe has been constructed to allow recordings of blood velocity to be made over several days. The Doppler unit was adapted to record the blood velocity automatically for 1 min every 30 min so keeping the level of exposure to ultrasound and quantity of recorded data down to a reasonable level. Volume flow measurement may also be obtained if the diameter of the graft is measured using an ultrasound scanner. The technique has the potential to provide useful information about blood flow changes in grafts as well as enabling early detection of graft failure. Examples of some of the recordings made will be given.

Computer-based system for feedback of obstetric ultrasound data and evaluation of ultrasonic measurement charts

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This study describes a new computer-based system for deriving feedback of obstetric and neonatal information for comparison with predictions from ultrasonic measurements. Details of over 800 scans of pregnant patients, including BPD and FL data, have been entered on to a BBC computer database. After a suitable delay the minicomputer containing obstetric Korner data is interrogated by software written to run on a BBC computer and relevant delivery and perinatal data transferred to complete the data entries. An analysis of the accuracy of the ultrasonic data in predicting delivery data has been performed using published tables and formulae from several authors.

Systematic errors of up to 1 week have been found in some cases. The system allows for a "local" table to be produced fitting local data. A figure of merit has been produced based on the accuracy and standard deviation to compare the value of any number of published tables.

Ultrasonic endoscope based on a low cost personal computer

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Ultrasound remains pre-eminent as a non-invasive technique for the investigation of internal tissue structure; however, there is a compromise in its use, between depth of penetration and resolution. For the study of the vascular system, both deep penetration and high resolution are required, and these cannot be achieved simultaneously using existing percutaneous ultrasonic probes. To overcome this problem, we have developed an ultrasonic endoscope, capable of producing high resolution images of vessel walls for the study of vascular structure and dynamics. This ultrasonic endoscope system is based on a low cost personal computer and a commercial pulsar/receiver. A rotating transducer is used for intravascular imaging, and the ultrasound echos are digitized, transferred to the computer and images displayed in real time on a video adapter board. Post-processing improves the signal-to-noise ratio and enhances viewing contrast. A PVDF-2 transducer, chosen for its small size (1 mm thick) and high bandwidth, is mounted at the end of a Bowden cable with its face parallel to the cable axis and rotated using a stepper motor. Ultrasound pulses are generated, and the echos digitized at 7.5 MHz with 6 bit resolution using a commercial ultrasound pulsar/receiver. Two hundred and fifty six samples per echo are transferred to a low cost IBM AT compatible personal computer through a parallel interface at the rate of 50 echos per revolution. Radial scan ultrasound images may be produced in real time (128 × 128 resolution) at a maximum rate of six per second, or data may be captured to memory at 10 revolutions per second, stored to disk and later displayed at full resolution (512 × 512). Spatial resolution is 0.2 mm, and a region of 50 mm diameter can be imaged. Data may also be viewed in A mode or M mode. A digital ultrasound system has a number of advantages compared with an analogue system: it is more flexible; it is easier and faster to develop; data can be more easily stored and replayed; and post-processing to enhance signal quality and feature extraction can be applied.

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Book reviews

Radiation Therapy of Head and Neck Cancer. Ed. by George E. Laramore, pp. xii + 237, 1989 (Springer-Verlag, Berlin Heidelberg), DM240.
ISBN 3–540–19360–X (Berlin)
0–387–19360–X (New York)

This is a book published by the Chairman of the Head and Neck Committee of the Radiation Therapy Oncology Group (RTOG) covering the management of cancer of the head and neck, with specific emphasis on the use of radiotherapy. In the preface the editor expresses the hope that the book provides a comprehensive review, suitable both for practising radiation oncologists and the resident in training. He aims for a balanced picture, including both the European and the North American approach to cancer. The book achieves at least part of its brief but, in a field where controversy is rampant, cannot achieve it all. Inevitably, there is a trend towards a North American view with relatively few references to the large European studies, particularly in hyperfractionation where the European Organization for Research and Treatment of Cancer (EORTC) have made great contributions.

The book is very nicely laid out, particularly for those about to take the final FRCR. Many of the controversies about management are aired, although the British radiotherapists may not always agree with the conclusions. Similarly, the various fractionation schedules are very North American, coming towards 1.8–2 Gy fractions with no mention of the Edinburgh–Toronto more accelerated regimes or results with "Manchester" fractionation.

I think this would be a useful reference book to have in a library, as its ordered presentation is ideal for both lectures and examinations and it has a reasonably comprehensive reference list. However, it is an expensive book for an individual to buy and will probably be reserved for enthusiasts in the field.

E. J. Maher

Multimodal Treatment of Ovarian Cancer. EORTC Vol. 20. Ed. by P. F. Conte, N. Ragni, R. Rosso and J. B. Vermorken, pp. xxii + 329, 1988 (Raven Press, New York), $111.50.
ISBN 0–88167–476–1

This book is Volume 20 in the Monograph series of the European Organization for Research and Treatment of Cancer (EORTC). It contains contributions from a large number of authors concerned with carcinoma of the ovary, with 37 chapters covering tumour biology, diagnosis of and staging early ovarian carcinoma, surgery, advanced ovarian carcinoma and new therapeutic modalities.

Camera ready format and the variation in the text detract from the appearance of the book. However, several chapters are particularly worthwhile and present comprehensive reviews of treatment modalities. In particular, the chapter on radiotherapy and ovarian cancer by Alan Denbow presents a good resumé of the work at the Princess Margaret Hospital, and the chapter by Gronoskow in Britain on radioimmuno-synography in ovarian cancer is similarly concise. A chapter by Professor Fox on ovarian tumour of borderline malignancy covers this very interesting and important area of ovarian pathology, and there are good reviews on both single agent and combination chemotherapy.

The book is marred by a few articles with little or no new information, and some are poorly written with many grammatical mistakes. As is the case with camera ready formats, the only illustrations are in the form of tables and a few diagrams. There are no pictures to illustrate any of the chapters referring to imaging techniques, which is a great disadvantage.

Many of these chapters are published elsewhere in slightly modified forms, and although this book may be useful as a reference book in a department treating large numbers of ovarian cancers, the coverage of the disease is too patchy, and of too varying a quality, for it to be regarded as a textbook on the treatment of ovarian cancer.

P. Blake

Pediatric Radiation Oncology. By E. C. Halperin, L. E. Kun, L. S. Constine and N. J. Tarbell, pp. xii + 434, 1989 (Raven Press, New York), $122.50.
ISBN 0–88167–547–4

This is a useful book for anyone concerned with the care of children with cancer. Because of the impact of chemotherapy in this area of oncology, most textbooks deal only briefly with the role of radiotherapy. Here is a text that systematically covers the cancers of childhood, giving a full picture of the epidemiology, pathology, diagnosis and treatment, but, in addition, addresses the question of the use and effects of radiation. While concentrating on the most common cancers, it is comprehensive in that it also gives fair weight to rarer tumours, and thus information that is otherwise difficult to come by.

The book is well set out, easy to read and extremely well referenced. However, it would have been useful to have some of the technical descriptions clarified by the use of good illustrations such as diagrams of field arrangements and dose distributions.

The inclusion of chapters on anaesthesia for external beam radiation and stabilizing devices is a good indication of the depth of understanding that the authors have of the subject and of their practical hands-on experience. Both are extremely useful, but tend to be omitted from formal textbooks. In addition, there is an excellent and detailed chapter on the late-effects of cancer treatment.

One draw-back to this book is its price. The copy reviewed was priced at $122.50 and no sterling price was given. At this cost, it is likely to have a distribution considerably more limited than it deserves.

Diana Tait

A Primer on Theory and Operation of Linear Accelerators in Radiation Therapy. By C. J. Karzmark and Robert J. Morton, pp. vi + 45, 1989 (Medical Physics Publishing Corporation, Madison, Wisconsin, USA), $12.
ISBN 0–944838–07–3

This booklet written by two distinguished American physicists was originally published by the US Bureau of Radiological Health and now appears in revised form. It lives up to its title and is easy to read with key words printed in bold type. There are plenty of diagrams to accompany the explanations, and some black and white photographs of particular examples.

The introduction describes how a medical accelerator is used, names its constituent parts and describes the movements possible. It then explains how the energy is defined, and describes the operation of an elementary linac. There is a brief comparison with diagnostic X-ray generators. The next section details the major modules and components of an operational linac. The use of microwaves to accelerate electrons is explained, together with the principles of microwave production. The text then follows on logically to describe standing and travelling wave accelerator structures. There is a new section of dual energy X-ray linear accelerators and the properties of the bending magnets required for these recent advances. Appendix A describes most medical linear accelerators currently on the market and illustrates some models. Appendix B gives the manufacturers' performance specifications in tabular form, so that different units can easily be compared. The booklet restricts itself to the traditional basics of linear accelerator design, and does not address the advances in microprocessor control, asymmetric and multisegment collimators, and automatic wedges.

It is intended for students of radiotherapy and oncology, physics and radiography. It fulfills this intention admirably and is a useful publication in a field where very little information at this introductory level is available. It is reasonably priced and I recommend it for the departmental library, or for personal use if you do not have the first edition.

HELEN MORGAN

Determination of Dose Equivalents from External Radiation Sources, Part 2. ICRU Report 43, pp. x + 51, 1988 (International Commission on Radiation Units and Measurements, Maryland, USA), $17.
ISBN 0-913394-33-5

This report is one of a series of three addressing the problems of determining dose-equivalents resulting from exposure to sources external to the body. The first part (Report 39) introduced new quantities to be employed in radiological protection monitoring of both the environment and the individual, namely ambient dose-equivalent (H*(d)), directional dose-equivalent (H′(d)) and individual dose-equivalent penetrating (H(d)) and superficial (H(d)). This second report in the series gives the reasons for the choice of these new quantities, with supporting physical data and information on their relationship with both organ and effective dose-equivalents. It is the intention of the Commission to issue a third report to provide guidance on the design, calibration and use of radiation protection instruments intended for measurements of these new quantities.

The International Commission on Radiation Units and Measurements (ICRU) Report 43 contains six sections and three appendices and considers photon, neutron and electron radiation. After a short introduction in section 1, section 2 outlines the reasoning behind the selection of the new quantities and this is further expanded in Appendix C. Section 3 outlines the calculated and experimental data from anthropomorphic phantoms and the ICRU sphere used as a basis for the evaluation and discussion of the new quantities. The data are presented in graphical form in Appendix B. Instrumental characteristics and calibration are discussed in section 4 and presumably this will be extended and expanded in the third report in the series. The last substantial section, chapter 5, presents the relationships between the new quantities and the organ and effective dose-equivalents defined in the International Commission on Radiological Protection (ICRP) Report 26 as the limiting quantities for dose restriction. The report concludes that "... the quantities will, hopefully, meet the needs of day-to-day operational practice while being acceptable to those concerned with metrological rigour, and they will be used to provide effective control consistent with current perceptions of the risks associated with exposure to ionizing radiations".

This report is a useful reference for the radiation physicist grappling with the problems of relating environmental measurements to dose-equivalent quantities defined in the present system of dose limitation. However, it is difficult to read the data from the small graphs with any accuracy and it is possible that ICRP Report 51, which contains much of the same data in tabular form, might prove to be the more useful reference.

ANNE WALKER

Tissue Substitutes in Radiation Dosimetry and Measurements. ICRU Report 44, pp. viii + 189, 1989 (International Commission on Radiation Units and Measurements, Maryland, USA).
ISBN 0-913394-38-6

Tissue substitutes are needed for the construction of phantoms, radiation detectors and as bolus materials in many areas of radiation science. In order to choose appropriate materials for each application it is necessary to have detailed information about the characteristics of tissue substitutes that affect radiation interactions. Report 44 provides this information and discusses the criteria governing its use.

The areas of radiation science are reviewed, and these include radiation dosimetry, radiotherapy, radiodiagnosis, radiation protection and radiobiology. There is a chapter on basic concepts describing the physical quantities that have to be considered for the radiation types considered, namely photons, electrons, neutrons and some heavy charged particles.

Chapters 3–5 discuss the physical characteristics of the most important human tissues for which substitutes are required; this includes tabulation of elemental composition, mass densities and electron densities. They also give recommendations for appropriate substitutes and comparisons of interaction and depth dose data for selected tissue substitutes.

Although the descriptive and explanatory chapters are very thorough, they occupy only 40 of the 186 pages of the report. The remainder consists of tabulated interaction data for 62 tissue substitutes, collated from several sources. It is potentially confusing that the source for electron stopping power data (Berger 1987) is different from that used in ICRU Report 37, particularly as no significant differences are apparent. One important omission is of data for Perspex (lucite, plexiglass or polymethylmethacrylate) which is a commonly used if not ideal material.

There is a short appendix on formulation and fabrication techniques that will not be needed by the average user of the report, and, as usual in ICRU reports, an extensive list of references.

P. C. WILLIAMS

Hospital Radiopharmacy Principles and Practice. IPSM Report No. 56. By M. Frier, J. G. Hardy, S. R. Hesselwood and R. Lawrence, pp. viii + 47, 1988 (Institute of Physical Sciences in Medicine, York), £8.50.
ISBN 0-904181-53-7

This small booklet of less than 50 pages packs in a great deal of useful information and advice about modern hospital radiopharmacy work. It is an update of the Hospital Physicists' Association Report No. 16, *The Hospital Preparation of Radiopharmaceuticals*.

The introduction usefully summarizes the legislative framework, regulations and various guidance notes which are relevant in the radiopharmacy, both from the pharmaceutical point of view and from that of radiation protection. The authors sum up: "the preparation of radiopharmaceuticals must take place in an environment where the risks of radioactive contamination and radiation exposure are acceptably low and the environment must be controlled such that the risks of microbial and particulate contamination of parenterally-administered products are minimized". The remaining five chapters set out to show how this can be done.

Chapter 2 deals with facilities for the preparation of radiopharmaceuticals, both closed and open procedures, and gives advice on laboratory design, work stations and fume cupboards. A third chapter details equipment and procedures for shielding, handling, monitoring of activity, dose calibration and record keeping. All these are covered in a practical manner but briefly and therefore without much discussion of alternative techniques and procedures. Quality control is, in the light of present topicality, very usefully covered though again detail is inevitably limited. Methods of chromatography, for example, are not dealt with in the detail that would allow the uninitiated to set up the method. This is inevitable in a small handbook of this nature, and the report is not intended to replace textbooks on the subject.

Discussing tests for pyrogens, the authors strike the right balance between the older but accepted rabbit test, which is largely irrelevant to nuclear medicine except for pre-testing sterile ingredients for kit work, and the Limulus lysate test, mentioning briefly its particular relevance and higher sensitivity for intrathecal preparations. This needs to be stressed as meningism following the introduction of small quantities of pyrogen during cerebrospinal fluid (CSF) studies is still a problem.

A section discussing sterility checks has a more practical approach (relevant to radiopharmacy) than as specified in the European Pharmacopoeia. However, the authors seem to be in favour of the membrane filtration technique which can involve more handling of radioactive pharmaceuticals as well as allowing greater opportunity for irrelevant contamination. They also advise broth transference tests in which a culture medium is used in a mock radiopharmaceutical production to test the aseptic technique of the operators. This, however, is of arguable value for routine testing as inevitably operators are going to be particularly careful when doing a sterility test run. It is a good method of checking that an operator has reached a necessary level of skill but not that it is maintained. It is just as easy to take an extra dose at random from a radiopharmaceutical production run and innoculate a suitable culture medium that can be incubated and suitably shielded in the radiopharmacy until, in a week or so, it can be safely transferred to a suitable laboratory for sterility testing: the dose prepared for the patient who failed to attend is an ideal source. For short-lived materials like technetium radiopharmaceuticals, process controls assume extra importance. These monitor the environment and check reliability of equipment involved in radiopharmaceutical production. The authors cover these with details of requirements for air supplies, filtration and calibration checks. A short chapter on radiation monitoring finishes off this small handbook.

The authors have not attempted to discuss the ultimate justification for the requirements that they specify to meet the regulations and guidance notes. Safety, in all its aspects, requires judgements on some sort of cost-benefit basis. Sometimes we use "safety" to get extra facilities which we feel we require but at other times we have "safety" thrust upon us! Safety measures take time, effort and money—particularly money. Whether the Health Service (and British taxpayers) get the best value for their money from safety measures is a difficult judgement. By following all the advice in the present booklet, you will produce "very safe" radiopharmaceuticals, but at a price.

One quite unfair criticism would be that the authors cover so much in this short report that it might be thought of as a substitute for a textbook of radiopharmacy. The authors are quite clear that it is not, and give a short list of useful references for further reading. This report should certainly be available in every radiopharmacy and would be particularly valuable for those proposing to extend their radiopharmaceutical facilities, whether it be just in the range of materials produced, or in new building and equipment.

D. H. Keeling

Diagnostic Ultrasound. Principles, Instruments and Exercises, 3rd edn. By Frederick W. Kremkau, pp. x + 364, 1989 (W. B. Saunders, Philadelphia), £27.
ISBN 0-7216-2823-0

Over 8 years ago, Dr Meire wrote a valuable review of the first edition of this book (BJR, *54*, 275), and much of what he said then remains entirely relevant for this third edition. As a basic ultrasound physics text, including many exercises to test the reader's understanding, it is a valuable introduction for novices, or for the more experienced user who may have difficulty understanding the technical basics. The third edition is over 70% longer than the first (and over twice the price). Useful additional material has been added describing imaging artefacts, Doppler ultrasound, performance evaluation and safety. Many grey-scale and a few colour images have been included.

The reader should be aware that even in this third edition a few residual textural errors occur, although these are mostly obvious misprints (e.g. ms for μs).

As a physicist, I was disappointed to find almost no reference to the widely used membrane pvdf hydrophones for exposure measurement, and a definition of a hydrophone as "a small transducer element mounted on the end of a narrow tube". However these are relatively minor criticisms, and I am sure that Dr Kremkau's book will continue to hold a well-deserved place in the education of the increasing numbers of those entering the world of medical ultrasound.

F. A. Duck

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Review article

Urinary tract infection in paediatrics: the role of diagnostic imaging

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Infection of the urinary tract (UTI) has several clinical subgroups, each requiring different degrees of investigation. The most severe, acute pyelonephritis, is characterized by ill health, anorexia, pyrexia (>38.5°C), an erythrocyte sedimentation rate greater than 20 mm/h or C-reactive protein greater than 10 mg/l, pyuria, bacteruria and possible septicaemia. The child may well require hospitalization and parenteral antibiotics. The term cystitis is used to refer to children with lower urinary tract symptoms but without systemic illness who have more than 100 000 bacteria per ml in the urine. They should be distinguished from children who are asymptomatic but nevertheless have positive urine cultures, *i.e.* asymptomatic bacteruria. This last group usually consists of girls over 5 years old and do not require much investigation. Clinically these three groups overlap to some extent, but nevertheless the presentation should be a guide to the choice of the appropriate imaging.

First proved urinary tract infection

Urinary tract infection is common: the imaging that children undergo is important in terms of resource utilization as well as discomfort and radiation exposure. A conscious effort must be made not to over-investigate the child or to overburden the radiology department, yet treatable disorders or potential long-term complications must be detected (Saxena et al, 1975; Asscher, 1980).

Clinical context

A prospective study by Dickson (1979) found 3.1/1000 girls and 1.7/1000 boys presented annually with a first symptomatic UTI. The incidence of end-stage renal failure due to pyelonephritis in Europe in individuals under 40 years of age is 4–5 per million per year (Broyer et al, 1984). Combining various data, Haycock (1986) estimated the risk of renal failure due to reflux nephropathy in children presenting with UTI as less than 1% for boys and less than 0.5% for girls. In part this risk arises from pyelonephritic scarring consequent upon UTI and in part from renal dysplasia associated with vesico-ureteric reflux (VUR). The probability that any child presenting with UTI is at risk from preventable renal failure is thus less than Haycock's estimate, perhaps six out of a million. Renal damage may result when UTI occurs either in the presence of obstruction, or under certain conditions when VUR is present. Scarring in association with VUR appears to depend on a number of factors: infection, intrarenal reflux and age. The young, especially those under 1 year of age are at greatest risk (Ransley & Risdon, 1975). Scarring in association with VUR is usually apparent at the initial investigation suggesting either that it occurred with the first UTI or that the appearances are a result of dysplasia before the time the child is first seen (Birmingham Reflux Study Group, 1987). The development of new scars has been described, but is rare, especially in the asymptomatic older child (Sherwood & Whitaker, 1984; Smellie et al, 1985). Urinary tract infection in the presence of an obstruction requires surgical treatment.

Clinical controversy

Most clinicians agree that with UTI and VUR, the age of the child is an important determinant of the risk of scarring. The kidney of young children (under 1 year of age) are most susceptible, whilst in children older than 5 years with normal kidneys, scarring very rarely develops, especially if the child is asymptomatic. The above ages, *e.g.* 1 and 5 years, are not accepted by all clinicians, some of whom feel that only the kidneys of children less than 2 years of age are at significant risk. One study suggested that only in asymptomatic children over 7 years of age was the risk of scarring with UTI no longer significant (Smellie et al, 1985). The greatest controversy concerns the child between these two age groups: is VUR the major anomaly to be excluded, or should one focus on the kidney? The logic is that if the kidney has not scarred after the first UTI, then it is unlikely to do so later on in this age group, so that the presence or absence of VUR may be unimportant.

Verber et al (1988) and Whyte et al (1988) both showed that it was only worthwhile looking for VUR in children with an abnormal kidney in this intervening age group; conversely there are children in this age group with VUR but without renal scars (White, 1989).

Selection of children for imaging

Children of either sex with their first proved UTI require imaging; the younger the child, the more important these investigations. The studies of Williams (1976) and Dickson (1979) have shown that only 18–24% of children with lower urinary tract symptoms actually have UTI, which suggests that the single most important way to avoid unnecessary investigations is to ensure that only those with a definite UTI are investigated.

Aims of imaging

Firstly: to diagnose an obstructive uropathy. With increasing use of antenatal ultrasound, many congenital obstructions are diagnosed *in utero*. This change in medical practice may alter the previous statistics which showed that 10% of children with UTI had an obstructive uropathy.

Secondly: to detect the presence of calculi.

Thirdly: to identify those children with existing renal damage who are at risk of long-term complications, such as hypertension or chronic renal failure.

Fourthly: to identify those children who are at risk of developing renal damage.

Finally: to monitor progress and the results of surgery.

Imaging controversy

Classically the diagnosis of renal scarring was based on the intravenous urogram (IVU) and that of VUR on contrast micturating cystourethrography (MCUG). Newer imaging techniques with lower degrees of invasiveness are widely available, and their role is being constantly appraised. There is little value in comparing a high quality IVU with an inadequate abdominal ultrasound (US) examination or ^{99}Tc^{m} dimercaptosuccinic acid (DMSA) scan. It is the responsibility of radiologists to ensure that good techniques (*e.g.* US, radionuclide cystography or ^{99}Tc^{m} DMSA scanning) do not develop bad reputations because of poor quality examinations. This article connot attempt to cover comprehensively imaging of the paediatric renal tract. It will focus on certain important aspects of each technique.

Ultrasound should diagnose all cases of obstructive uropathy, the majority of calculi and the presence of a small kidney. Renal length can be measured accurately by US in the majority of children and longitudinal examinations provide evidence of renal growth. A full US examination includes views of the bladder and the area behind the bladder. It is prudent to begin the US examination with views of the bladder in the younger child since micturition may occur during the examination, preventing evaluation of the lower ureters later. Numerous studies have shown the high sensitivity and specificity of US as a screening procedure for children with UTI compared with the IVU (Jaquier et al, 1983; Sherwood & Whitaker, 1984; Kangarloo et al, 1985; Whyte et al, 1988). If scarring is detected on US then there is no reason to doubt its existence but a normal US does not exclude a renal scar.

The IVU in children under 2 years of age may not provide sufficient anatomical detail, since high quality radiographs are difficult to obtain. The presence of bowel gas may obscure the calyces. Thus it is important to ensure quality of the US and ^{99}Tc^{m} DMSA scans.

A recent survey showed that 76% of paediatricians in England had access to radionuclide facilities but the survey implied that this facility was not fully used (Smyth et al, 1988). The ^{99}Tc^{m} DMSA scan is a sensitive technique to detect a renal scar; recent studies support the early impression of the high sensitivity of the ^{99}Tc^{m} DMSA in the detection of a renal scar (Merrick et al, 1980; Stroller & Kogan, 1986; Goldraich et al, 1989). The initial IVU missed most of the scarring compared with ^{99}Tc^{m} DMSA in children between 0 and 6 years (Goldraich et al, 1989). This not surprising considering that this is the age when it is most difficult to obtain a high quality IVU. Most studies show that the ^{99}Tc^{m} DMSA scan does have a false negative rate (Smellie et al, 1988), but this is small compared with the false negative rate for the IVU. The time necessary for the development of a renal scar is unclear; using the IVU the shortest time recorded is 8–9 months, by Smellie et al (1975) and Hugosson et al (1976). Hodson and Wilson (1965) suggested that bipolar scarring took 16 months to develop, while Filly et al (1974) suggested that 2 years could be required in certain cases. Using ^{99}Tc^{m} DMSA, Monsour et al (1987) showed that 25% of kidneys had photon-deficient areas if scanned during the first month after the UTI, while at 6 months only 4% still had defects which could now be called scars, and Goldraich et al (1989) found that ^{99}Tc^{m} DMSA scans in five children with UTI were abnormal during the infection but only one remained abnormal 4 weeks later. Parkhouse et al (1989) showed a similar time course in experimental UTI in the pig using ^{99}Tc^{m} DMSA. However, Verber et al (1988) found that 80% of all defects remain unchanged on follow-up ^{99}Tc^{m} DMSA scan in a selected group of children. It seems that ^{99}Tc^{m} DMSA scans show scars earlier than IVU, but should not be done within 4 weeks of the UTI.

The MCUG has been suggested as the first line imaging investigation in UTI (Blickman et al, 1985), but the information provided is restricted to the bladder, bladder emptying and VUR. Some clinicians state that the urethra in boys must be visualized in order to exclude bladder outlet obstruction, yet no study has compared the results of a comprehensive US examination (including full and empty bladder views) with the results of MCUG in the same boys. Renal reflux may be detected using radionuclide cystography with a reduction of radiation exposure by a factor of 20 compared with the MCUG (Rothwell et al, 1977). In the toilet trained child an indirect radionuclide cystogram (IRC), without the need for bladder catheterization, can be carried out using ^{99}Tc^{m} mercapto acetyl triglycine (^{99}Tc^{m} MAG3), when inclusion of the dynamic phase of the renal scan provides information on individual kidney function. If the volume and radioactivity of the voided urine is measured, the IRC can provide premicturition bladder volume, residual volume, peak flow rate and, if renal reflux is seen, this can be quantified (van der Vis-Melsen et al, 1989).

In the younger child (*i.e.* not toilet trained) a direct radionuclide cystogram (DRC) which requires a bladder catheter (a procedure similar to the classical MCUG) may be undertaken. The results of the DRC may also be quantified (Willi & Treves, 1985). The DRC has a high sensitivity compared with the MCUG (Conway & Kruglik, 1976; Willi & Treves, 1985), as does the IRC (Handmaker et al, 1973; Pollet et al, 1981; Bower et al, 1985; Nielsen et al, 1985; Carlsen et al, 1986; Chapman et al, 1988). Few studies have been reported with poor results of the IRC (Majd, 1986). Radioisotopic imaging procedures do not increase radiation exposure.

Time is required before full assessment of any new technique can take place. The US images are best interpreted by the radiologist who did the examination, particularly as lack of anatomical landmarks adds difficulty to remote interpretation. Radionuclides provide functional information in the form of both images and numbers/graphs. Radiological anatomical detail is lacking and therefore certain clinicians are sceptical in accepting the high sensitivity of the gamma camera in detecting small abnormalities. These factors add to the hesitation some radiologists and clinicians feel towards either US and/or radionuclide studies. An increasing number of articles suggest that in institutions with high quality US and radioisotope facilities, the well trusted IVU and MCUG may be displaced as first line investigations in certain children with a UTI. A possible result is over-investigation of children with UTI (Whyte et al, 1988). Medical audit is now an accepted concept, which with divergent approaches between radiologists about investigation of UTI, should allow assessment of different imaging techniques and responsible use of resources (Diament, 1988). An example is the value of the plain abdominal film in children under 2 years of age, which is considered by some paediatric radiologists to be essential, yet there is no study validating this point. Preliminary results of a study at four paediatric centres in Britain suggest that no significant urological or skeletal abnormality would have been missed in over 600 children of all ages if the plain abdominal radiograph had been excluded from the initial imaging sequence (Kenney, 1989). Mention has been made of the different quality of certain investigations: surely it is up to radiologists (including US, nuclear medicine, etc.) as a group to ensure that all the examinations done are diagnostic!

Table II

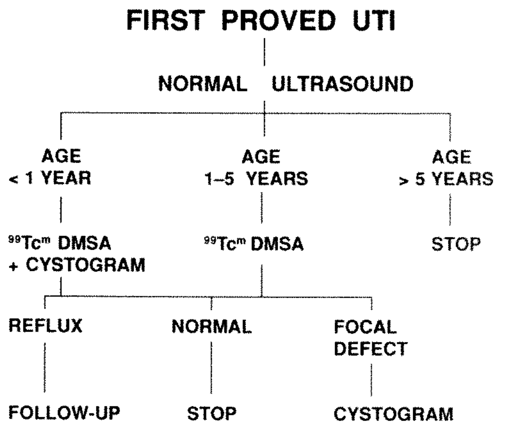


Table I

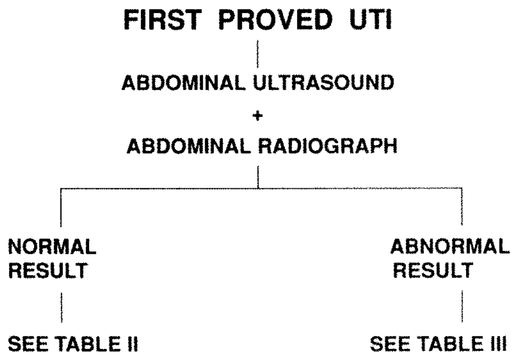
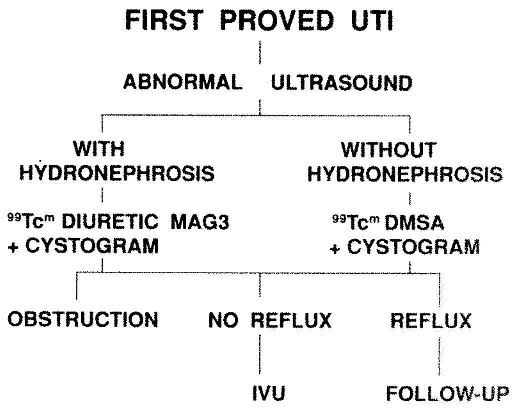


Table III



Protocol for the first documented UTI (Tables I–III)

The purpose of a protocol is to focus the attention of the medical team to ensure that the protocol fits the child and not that the child is forced to fit the protocol.

Currently all children with UTI shoud have a plain abdominal radiograph as well as an US of the kidneys and bladder to exclude urinary calculi, nephrocalcinosis and obstructive uropathy, as well as to measure the renal size (Jaquier et al, 1983; Sherwood & Whitaker, 1984; Kangarloo et al, 1985; Whyte et al, 1980). If the US is normal then no further investigations should be undertaken in children older than 5 years. The susceptibility of the kidney to damage from VUR and UTI in infants under 1 year old means that both VUR and renal scars should be positively excluded. This requires both a cystogram and $^{99}\text{Tc}^{m}$ DMSA scan. In girls, a DRC may be carried out, but in boys, a MCUG is required.

In the child between 1 and 5 years of age there is no general agreement. One suggested pathway is a $^{99}\text{Tc}^{m}$ DMSA at 1–4 months after the UTI to identify an abnormal kidney; if abnormal the child requires a cystogram. If the $^{99}\text{Tc}^{m}$ DMSA is normal then it is appropriate to wait for any second UTI before undertaking further investigation. An alternative pathway is to carry out a cystogram, and then stop if no VUR is detected; if VUR is seen then a $^{99}\text{Tc}^{m}$ DMSA scan would be required to assess the extent of any renal damage.

Vesico-ureteric reflux should be excluded in infants with a family history of VUR or reflux nephropathy. This should be done in the neonatal period before any UTI has occurred. If VUR is detected then a $^{99}\text{Tc}^{m}$ DMSA scan should be undertaken at about 3 months of age while the infant is on a prophylactic urinary antiseptic. If a $^{99}\text{Tc}^{m}$ DMSA scan is carried out at a younger age, renal immaturity may make detection of scars difficult.

Long-term follow-up

All children with VUR and an abnormal kidney require long-term follow-up irrespective of their age because of the increased incidence of hypertension and the occasional development of chronic renal failure. Many children with VUR will be placed on long-term antibiotic prophylaxis; if cessation of VUR is a prerequisite to stop this treatment then re-evaluation for VUR should be done with a radioisotope cystogram (either DRC in the younger child or IRC in the toilet trained child). If ureteric reimplantation has been undertaken then an US and $^{99}\text{Tc}^{m}$ MAG3 isotope scan are required to exclude obstruction following surgery, and to show that renal reflux has been prevented. Children with a scarred kidney require regular blood pressure monitoring with infrequent but regular imaging.

Recurrent or breakthrough symptomatic UTI

If US has shown that both kidneys are normal, then in older children (more than 5 years), the possibility of renal damage is very small (Smellie et al, 1985) and further imaging is that of a second UTI, *i.e* a repeat comprehensive US (including images of the bladder pre- and post-micturition) and an IRC (assessing renal function excluding renal reflux). With a further symptomatic UTI then an IVU with another comprehensive US should be done to exclude unusual pathology.

The younger child (between 1 and 5 years) with normal kidneys and known VUR requires a repeat cystogram to assess if the reflux has stopped since some clinicians will consider surgery to stop VUR (reimplantation or periureteric injection therapy, *i.e.* "Sting") in this situation. The younger the child, the more inclined one would be to repeat the $^{99}\text{Tc}^{m}$ DMSA in the presence of VUR and breakthrough infection. Progressive renal damage in previously scarred kidneys has been well documented. Verber and Meller (1988) showed that all children with progressive renal damage had breakthrough infections in the presence of VUR. These infections require prompt treatment and require that the child returns to the radiology department for further imaging to assess the VUR and the extent of the renal damage on $^{99}\text{Tc}^{m}$ DMSA.

Acute phylonephritis

This manifestation of UTI requires imaging of both the upper and lower renal tract. The US may show a large "bright" kidney compared with the opposite side, or may be normal (Christophe et al, 1983). On the $^{99}\text{Tc}^{m}$ DMSA scan the entire kidney functions poorly with additional photon deficient areas. Computerized tomography (CT) shows a large kidney with no enhancement of focally affected areas following intravenous contrast medium. Progress of the condition should be monitored by US with either $^{99}\text{Tc}^{m}$ DMSA scan or CT scan. The use of the IVU has been rather disappointing. Reflux must be positively excluded; in girls a radioisotope cystogram is sufficient while in boys, the urologist who demands to see the urethra will press for a MCUG.

Conclusion

The first proved UTI in any child requires investigation. All children should have a US and plain abdominal radiograph. Children under 1 year of age also require a MCUG and $^{99}\text{Tc}^{m}$ DMSA scan. Children over 5 years of age do not require further imaging. Children aged between 1 and 5 years require a $^{99}\text{Tc}^{m}$ DMSA scan and/or a cystogram, with choice of procedure currently varying with different clinical opinions. All follow-up cystography for VUR should be with radionuclides.

References

Asscher, W. A., 1980. *Sequelae of Urinary Tract Infection. The Challenge of Urinary Tract Infections* (Academic Press, London), pp. 112–128.

Birmingham Reflux Study Group, 1987. Prospective trial of operative versus non-operative treatment of severe reflux in childhood: five years' observation. *British Medical Journal, 295*, 237–241.

Blickman, J. G., Taylor, G. A. & Lobowitz, R. L., 1985. Voiding cystourethrography: the initial radiologic study in children with urinary tract infection. *Radiology, 156*, 659–662.

Bower, G., Lovegrove, F. T., Geijsel, H., van der Scaff, A. & Guelfi, G., 1985. Comparison of direct and indirect radionuclide cystography. *Journal of Nuclear Medicine, 26,* 465–468.

Broyer, M., Rizzoni, G., Brunner, F. P., Brynger, H., Challah, S., Grety, N., Jacobs, C., Kramer, P., Selwood, N. H. & Wing, A. J., 1984. Combined report on regular dialysis and transplantation of children in Europe. *XIV Proceedings of the European Dialysis and Transplant Association, 5,* 55–79.

Carlsen, O., Lukman, B. & Nathan, E., 1986. Indirect radionuclide renocystography for determination of vesico-ureteral reflux in children. *European Journal of Nuclear Medicine, 12,* 205–210.

Chapman, S. J., Chantler, C., Haycock, G. B., Maisey, M. N. & Saxton, H. M., 1988. Radionuclide cystography in vesico-ureteric reflux. *Archives of Disease in Childhood, 63,* 650–651.

Christophe, C., Bogaert, C., Spehl, M. & Kramer-Permulter, N., 1983. Ultrasound of pyelonephritis. *Pediatrics, 13,* 173.

Conway, J. J. & Kruglik, G. D., 1976. Effectiveness of direct and indirect radionuclide cystography in detecting vesicoureteral reflux. *Journal of Nuclear Medicine, 17,* 81–83.

Diament, M. J., 1988. Is ultrasound screening for urinary tract infection cost effective? *Pediatric Radiology, 18,* 157–159.

Dickson, J. A., 1979. Incidence and outcome of symptomatic urinary tract infection in children. *British Medical Journal, i,* 1330–1332.

Filly, R. A., Friedland, G. W., Goven, D. E. & Fair, W. R., 1974. Development and progression of clubbing and scarring in children with recurrent urinary tract infection. *Radiology, 113,* 145–153.

Goldraich, N. P., Ramos, O. L. & Goldraich, I. H., 1989. Urography versus DMSA scan in children with vesicoureteric reflux. *Pediatric Nephrology, 3,* 1–5.

Haycock, G. B., 1986. Investigation of urinary tract infection. *Archives of Disease in Childhood, 12,* 1155–1158.

Handmaker, H., McRae, J. & Buck, E. G., 1973. Intravenous radionuclide voiding cystography (IRVC). *Radiology, 108,* 703–705.

Hodson, C. J. & Wilson, S., 1965. Natural history of chronic pyelonephritic scarring. *British Medical Journal, 2,* 191–194.

Hugosson, C. O., Chrispin, A. R. & Wolverson, M. K., 1976. The advent of the pyelonephrotic scar. *Annals of Radiology, 19,* 1–6.

Jaquier, S., Borges, M., Forbes, P. & Nogrady, M. B., 1983. The value of ultrasound examination as a screening procedure in first documented urinary tract infection in children. *Pediatric Radiology, 13,* 173.

Kangarloo, H., Gold, R. H., Fine, R. N. & Diament, M. J., 1985. Urinary tract infection in infants and children evaluated by ultrasound. *Radiology, 155,* 367–374.

Kenney, I., 1989. Personal communication.

Majd, M., 1986. Comparison of direct and indirect isotope cystography. *Radiology, 158,* 228.

Merrick, M., Uttley, W. S. & Wild, S. R., 1980. The detection of pyelonephritic scarring in children by isotope imaging. *British Journal of Radiology, 53,* 544–556.

Monsour, M., Azmy, A. F. & MacKenzie, J. R., 1987. Renal scarring secondary to VUR. Critical assessment and new grading. *British Journal of Urology, 60,* 320–324.

Nielsen, J. B., Jensen, F. T., Munch, J. T., Charles, P. & Djurhuis, J. C., 1985. The diagnosis of vesico-ureteral reflux. Radiologic and medicine methods. *Scandinavian Journal of Urology and Nephrology, 19,* 109–112.

Parkhouse, H. F., Godley, M. L., Cooper, J., Risdon, R. A. & Ransley, P. G., 1989. Renal imaging with Tc 99m DMSA in the detection of acute pyelonephritis: an experimental study in the pig. *Nuclear Medicine Communications, 10,* 63–70.

Pollet, J. E., Sharp, P. F., Smith, F. W., Davidson, A. I. & Miller, S. S., 1981. Intravenous radionclide cystography for the detection of vesico-renal reflux. *Journal of Urology, 125,* 75–78.

Ransley, P. G. & Risdon, R. A., 1975. Papillary morphology in infants and young children. *Urology Research, 3,* 111–113.

Rothwell, D. L., Constable, A. R., & Albrecht, M., 1977. Radionuclide cystography in the investigation of vesico-ureteric reflux in children. *Lancet, i,* 1072–1075.

Saxena, S. R., Lawrence, B. M. & Shaw, D. G., 1975. The justification for early radiological investigation of urinary tract in children. *Lancet, ii,* 403.

Sherwood, T. & Whitaker, R. H., 1984. Initial screening of children with urinary tract infections: is plain film radiography and ultrasound enough? *British Medical Journal, 288,* 827.

Smellie, J. M., Edwards, D., Hunter, N., Normand, I. C. S. & Prescod, N., 1975. Vesico-ureteric reflux and renal scarring. *Kidney International, 8,* s65–s72.

Smellie, J. M., Ransley, P. G., Normand, I. C. S., Prescod, N. & Edwards, D., 1985. Development of new renal scars: a collaborative study. *British Medical Journal, 290,* 1957–1960.

Smellie, J. M., Shaw, P. J., Prescod, N. P. & Bantock, H. M., 1988. 99m Tc DMSA scan in patients with established radiological scarring. *Archives of Disease in Childhood, 63,* 1315–1319.

Smyth, R. L., Berman, L. & Valman, H. B., 1988. Current practice in managing urinary tract infection in children. *British Medical Journal, 297,* 1516–1517.

Stroller, M. L. & Kogan, B. A., 1986. Sensitivity of Tc 99m DMSA for the diagnosis of chronic pyelonephritis: Clinical and theoretical considerations. *Journal of Urology, 135,* 977–980.

van der Vis-Melsen, M. J. E., Baert, R. J. M., Rajnherc, J. R. et al, 1989. Scintigraphic assessment of lower urinary tract function in children with and without outflow tract obstruction. *British Journal of Urology, 64,* 263–269.

Verber, I. G., Strudley, M. R. & Meller, S. T., 1988. 99m Tc DMSA scan as first investigation of urinary tract infection. *Archives of Disease in Childhood, 63,* 1302–1325.

White, R. H. R., 1989. Vesicoureteric reflux and renal scarring. *Archives of Disease in Childhood, 64,* 407–412.

Whyte, K. M., Abbot, G. D., Kennedy, J. C. & Maling, T. M. J., 1988. A protocol for the investigation of infants and children with urinary tract infection. *Clinical Radiology, 39,* 278–280.

Williams, C. M., 1976. Urinary tract infection in children: general practice survey. *Aust. Fam. Physician, 5,* 340–344.

Willi, U. V. & Treves, S. T., 1985. Radionuclide voiding cystography. In *Paediatric Nuclear Medicine,* ed. by S. T. Treves, (Springer-Verlag, New York), p. 105.

1990, *The British Journal of Radiology*, *63*, 512–516

Imaging for cochlear implants

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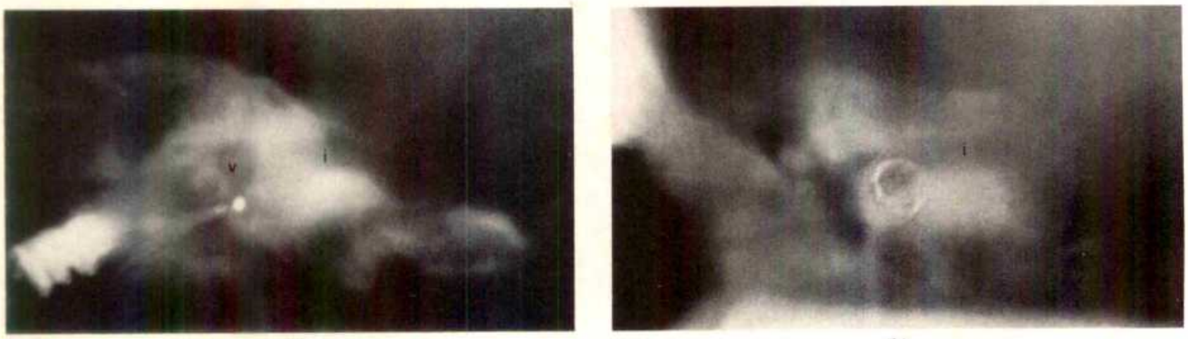
Abstract. Insertion of a sound amplification device into the round window niche (extracochlear implant) or into the coils of the cochlea (intracochlear implant) can give significant benefits to some carefully selected, severely deaf patients. Imaging has an essential role in selective and pre-operative assessment. Severe otosclerosis and post-meningitic labyrinthitis ossificans are common causes of deafness in these patients and can be demonstrated by computed tomography (CT). The most suitable side for operation can be assessed. We describe our experiences with 165 patients, 69 of whom were found suitable for implants. Thin (1 mm) section CT in axial and coronal planes is the best imaging investigation of the petrous temporal bones but the place of magnetic resonance scanning to confirm that the inner ear is fluid-filled and polytomography to show a multichannel implant in the cochlea is discussed. No implants were used for congenital deformities, but some observations are made of this type of structural deformity of the inner ear.

Conventional hearing aids amplify sound which is transmitted to the cochlea via the normal conducting mechanism of the eardrum and ossicular chain or, with bone conduction aids, by transmitting directly through the skull. Advances in modern electronics have made it possible to project sound further into the auditory reception pathway with significant benefit in carefully selected cases of severe deafness. Such devices are referred to as cochlear implants and those in current usage fall, broadly speaking, into two categories: the extracochlear *single channel electrode*, which is inserted into the round window niche, and the intracochlear *single channel* or *multichannel* implant in which an array of electrodes is threaded into the cochlea via the round window ideally reaching as far as the second coil (Fig. 1).

Radiology has a most important part to play particularly in the pre-operative selection of suitable subjects for cochlear implants and, to a lesser extent, in the follow-up. Implanting has proved most successful in post-lingual deafness, *i.e.* the small group of people who have become severely deaf after speech acquisition. Unfortunately, some of these disease processes not only damage the membraneous labyrinth but also result in sclerosis and new bone formation in the sites of prospective implantation inhibiting or precluding insertion of the electrode. Previous publications have stressed the high incidence of abnormalities of the inner ear that can be recognized by imaging (Harnsberger et al, 1987; Mueller et al, 1989).

Thin section imaging of the highest quality is obviously necessary and, as we found a similar high incidence of middle and inner ear abnormalities, an account of our experiences and recommendations seemed appropriate as more implant programmes are planned in Great Britain.



(a) (b)

Figure 1. Post-implant coronal polytomography showing (a) single channel extracochlear electrode in the round window niche, (b) multichannel electrode in the coils of the cochlea. Conventional tomography appears more satisfactory than CT for showing the device in position. (v = vestibule; i = internal auditory meatus.)

Materials and methods

One hundred and sixty-five patients from the University College Hospital, the Royal National Institute for the Deaf and more recently from the Cambridge Cochlear Implant Programmes have been assessed both clinically and radiologically, and 69 were judged suitable for implants. Fifty-one patients have been given implants, 18 are waiting. Extracochlear single channel implants were inserted in 59 and an intracochlear multichannel implant in two patients. Radiological assessment was initially by polytomography and, more recently, by thin section 1 mm high-resolution computed tomography (CT) with the pictures processed on a bone algorithm. Post-operative imaging has been confined to polytomography for one multichannel implant (Fig. 1) and two single channel electrodes. We have not used magnetic resonance (MR) in the pre-operative assessment.

The CT examination was done in axial and coronal planes to demonstrate cochlear coils, oval and round windows and the internal auditory meatus (Fig. 2). The facial recess and sinus tympani in the posterior aspect of the middle ear cavity were assessed on the same sections to ensure that there was adequate room for the surgeon to approach the round window niche. Mastoid pneumatization was also shown clearly on these sections. Abnormal soft-tissue opacification in the hypotympanum as from previous middle ear infection can also be shown and may inhibit the procedure.

Results

The pathogenesis of the deafness may be known or suspected from the history and clinical findings, but in four cases we were able to confirm that long standing hearing loss was due to undiagnosed otosclerosis/otospongiosis.

There were no subjects with congenital deafness in our programmes, and those with significant pathology shown by imaging fell into the two groups of post-meningitic labyrinthitis ossificans (also called obliterans), where new bone formation narrows or obliterates parts of the inner ear, and severe otosclerosis, which similarly encroaches upon the lumen of the labyrinth. One patient with post-meningitic labyrinthitis obliterans appeared to have the relevant parts of the inner ear unaffected but was rejected from the programme because of a congenital bone dysplasia which deformed the middle ear cavity (Fig. 3). Four patients were rejected from the programme because of the radiological findings.

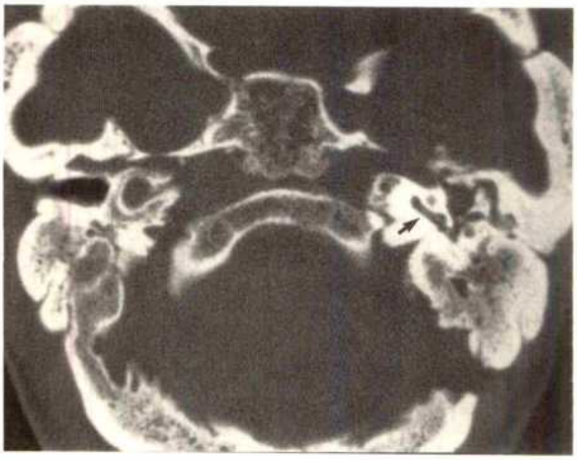
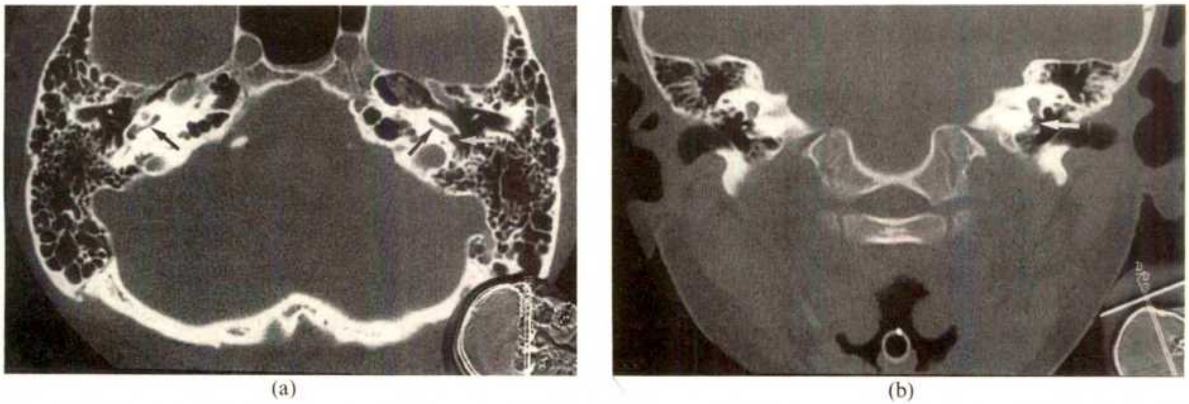


Figure 3. A patient with a sclerosing bone dysplasia of the skull, who had lost her hearing as a result of meningitis. The right ear showed evidence of labyrinthitis ossificans although the left cochlea was radiologically normal (arrow). However, the bone dysplasia had encroached on the middle ear which is fluid filled. Note the normal ossicles in this axial section.

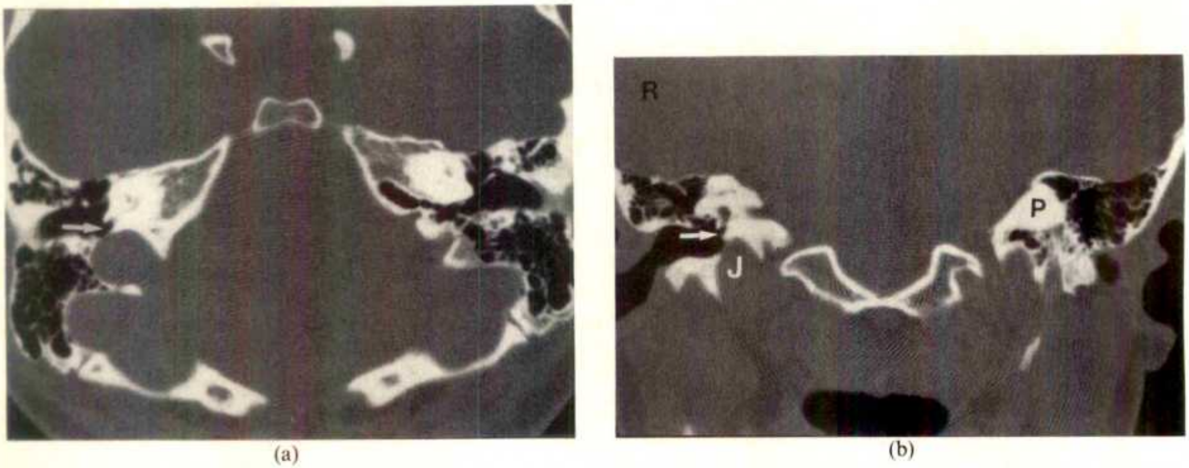
Discussion

Congenital abnormalities of the inner ear do not usually have progressive deafness and are therefore rarely suitable for implants as they do not have total, or near total, deafness allied to remembered speech ability. Exceptions would be the two types of deformity first



(a) (b)

Figure 2. High resolution CT in (a) axial and (b) coronal planes to show the round window niche (white arrows) and the hook and full length of the basal cochlear coil in the axial plane (black arrows).

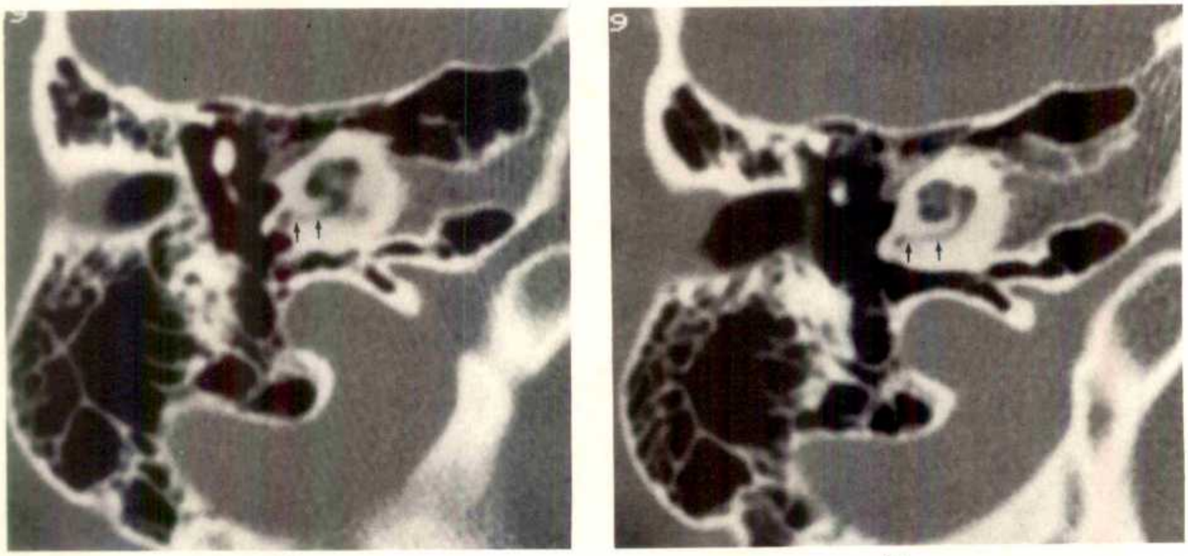


(a) (b)

Figure 4. (a) Axial and (b) coronal CT sections showing severe labyrinthitis ossificans. Only a faint outline of the cochlea coils can be seen on the axial section. The arrow indicates a patent round window niche on the right side only. Note also the proximity of the high anterior jugular fossa (J) on the right side and obliteration of the posterior semicircular canal (P) on the left.

described by Mondini (1791), namely deficient cochlea with normal basal turn and distal sac and a dilated vestibular aqueduct, both of which separately or in combination may be associated with fluctuant or progressive hearing loss. At least one case with such Mondini cochleas has had a successful multichannel implant (Silverstein et al, 1988). The more severe type of dysplasias with an amorphous cochlear sac, tapered internal auditory meatus (IAM) and risk of a cerebrospinal fistula (Phelps, 1987) would not be suitable for implantation as it is doubtful if a cochlear nerve is present. Cochleas which are smaller than normal are difficult to implant (Mueller et al, 1989) and this would seem to preclude multichannel electrodes for cases of ear pits deafness syndrome in which there is a reduced cochlea (Slack & Phelps, 1985). A narrow IAM also suggests absence of the stato-acoustic nerve and is a contra-indication to implantation (Shelton et al, 1989).

Labyrinthine ossification is the end result of suppurative labyrinthitis which may follow middle ear infection, meningitis or, rarely, septicaemia. The lumen of the labyrinth is narrowed or obliterated although very



(a) (b)

Figure 5. Two adjacent 1 mm axial CT sections 1 mm apart through the round window niche hook and full length of the basal turn of the cochlea. The narrowed segment (arrows) was a result of ossification of the scala tympani which necessitated drilling for 3 mm. Two sections are shown to confirm that the reduced lumen represented genuine narrowing and not just an eccentric slice. Note the chain of aircells behind the cochlea. (Patient of Mr Roger Gray.)

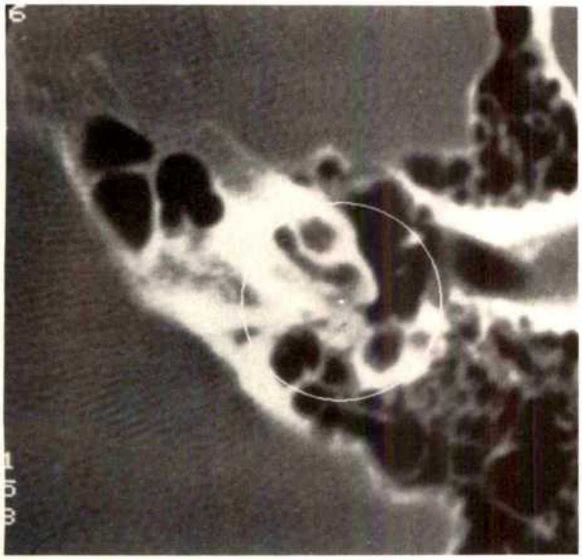


Figure 6. Otospongiosis adjacent to the basal coil particularly obliterates the round window. The white dot represents a densitometric reading of 580 HU as opposed to normal readings for the otic capsule of 2000–2400 Hounsfield Units.

rarely totally (Fig. 4). This can be assessed reliably by thin section CT, although considerable experience of petrous bone CT is required because of problems with partial volume averaging. Accurate appraisal of the cochlear coils is vital as a prelude to insertion of an intracochlear device (Jackler et al, 1987). Partial or complete obliteration of the cochlear coils by labyrinthitis ossificans would seem to us to be a contra-indication to a multichannel implant but at least one successful implantation appears to have been done by drilling out an artificial channel for the electrode to wrap around the modiolus (Gantz et al, 1988). One case in the Cambridge series had a successful multichannel implant although ossification of the scala tympani necessitated drilling for 3 mm until the fully patent cochlear duct was reached (Fig. 5).

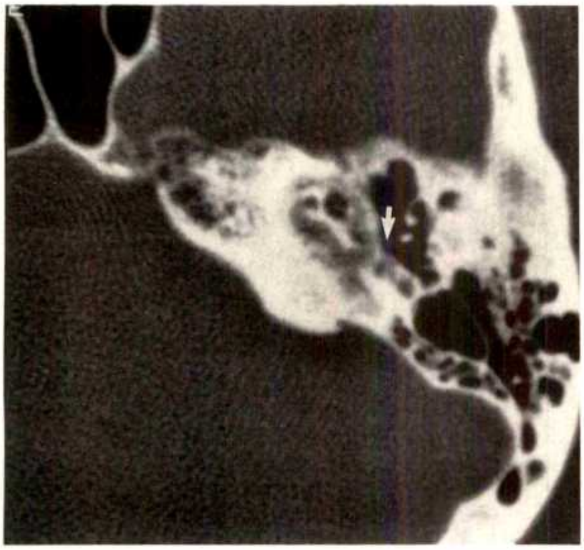


Figure 7. Severe mixed otosclerosis/otospongiosis gives a ring of rarefaction around the cochlea which is greatly reduced by otosclerotic bone. Note the involvement of the stapes crura (arrow).

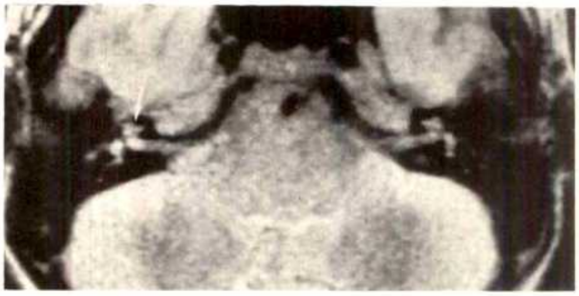


Figure 8. The individual coils of the cochlea are shown on this normal T_2-weighted axial MR scan (SE 2000/70). The bright signal confirms only that the coils are fluid filled.

Otosclerosis is not necessarily a contra-indication to cochlear implantation. In patients with fenestral otosclerosis, a bone plug in the round window can be successfully drilled and implantation can be performed if the surgeon knows, on the basis of CT findings, that the basal turn of the cochlea is patent beyond the obliterated round window (Harnsberger et al, 1987) (Fig. 6). Computed tomography of severe cases of otosclerosis often shows mixed otosclerosis and otospongiosis encroaching on the cochlear lumen. The border between the lumen and the rarefied bone may be difficult to assess if the zonal otospongiosis is severe (Fig. 7).

There are two other important features assessed easily on the pre-operative CT: (i) the position of the jugular bulb which if high and anteriorly placed may reach up almost to the round window niche (Fig. 4); (ii) the presence of a retro- and infra-cochlear chain of aircells (Fig. 5). These may be mistaken for the round window niche and attempts made to introduce the electrode into aircells rather than the round window niche.

Magnetic resonance may be a useful adjunct to CT but ideally requires appropriate surface coils to increase spatial resolution for the small area of the petrous pyramid under investigation. It is theoretically possible to tell whether the cochlear coils contain fluid or fibrous tissue from the strength of the signal on T_2-weighted sequences (Fig. 8) as well as confirming the presence of a stato-acoustic nerve. It is said that degeneration in the nerve will be revealed by a brighter than usual signal on T_1-weighted images (Valvassori, 1987). It is likely that future development programmes, both in this country and worldwide, will tend towards more intracochlear implants and the importance of MRI in the pre-operative assessment will increase.

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References

GANTZ, B. J., McCABE, B. F. & TYLER, R. S., 1988. Use of multichannel cochlear implants in obstructed and obliterated cochleas. *Otolaryngology Head and Neck Surgery*, *98*, 72–81.

HARNSBERGER, H. R., DART, D. J., PARKIN, J. L., SMOKER, W. R. K. & OSBORN, A. G., 1987. Cochlear implant candidates: Assessment with CT and MR imaging. *Radiology*, *164*, 53–57.

JACKLER, R. K., LUXFORD, W. M., SCHINDLER, R. A. & McKERROW, W. S., 1987. Cochlear patency problems in cochlear implantation. *Laryngoscope*, *97*, 801–805.

MONDINI, C., 1791. Anatomica surdi nati sectio, Bononiensi Scientarium et artium instituto atque academia commentarii. *Bonaniae*, *VII*, 419–428.

MUELLER, D. P., DOLAN, K. D. & GANTZ, B. J., 1989. Temporal bone computed tomography in the preoperative evaluation for cochlear implantation. *Annals of Otology, Rhinology & Laryngology*, *98*, 346–349.

PHELPS, P. D., 1986. Congenital cerebrospinal fluid fistulae of the petrous temporal bone. *Clinical Otolaryngology*, *11*, 79–92.

SHELTON, C., LUXFORD, W. M., TONOKAWA, L. L. & LO, W. W. M., 1989. The narrow internal auditory canal in children: A contraindication to cochlear implants. *Otolaryngology Head and Neck Surgery*, *100*, 227–231.

SILVERSTEIN, H., SMOUHA, E. & MORGAN, N., 1988. Multichannel cochlear implantation in a patient with bilateral Mondini deformities. *The American Journal of Otology*, *9*, 451–454.

SLACK, R. W. T. & PHELPS, P. D., 1985. Familial mixed deafness with branchial arch defects (earpits deafness syndrome). *Clinical Otolaryngology*, *10*, 271–277.

VALVASSORI, G. E., 1987. Workshop: Surgical anatomy and radiographic imaging of cochlear implant surgery. *American Journal of Otology*, *8*, 195–200.

1990, *The British Journal of Radiology*, *63*, 517–522

Initial experience with percutaneous transluminal angioplasty in the management of Takayasu's arteritis

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Abstract. We have performed percutaneous transluminal angioplasty (PTA) for 15 arterial stenoses in 11 patients with Takayasu's arteritis. The lesions included tight, proximally located renal artery stenosis (12 stenoses; nine patients), localized abdominal aortic stenosis (two patients) and occluded left common iliac artery (one patient). Clinically successful dilatation was achieved in seven patients (10 stenoses) with renal artery stenosis, in both the patients with abdominal aortic stenosis and in the only patient with an occluded left common iliac artery. No complications related to the procedure were encountered. The follow-up period ($n=7$) ranged between 1 and 16 months, mean follow-up period after renal angioplasty was 5 months and after abdominal aortic angioplasty was 12.5 months. Initial success has been maintained in both the patients with abdominal aortic stenoses and in four out of five patients with renal artery stenosis. Percutaneous transluminal angioplasty offers an attractive alternative for the management of stenosing lesions in Takayasu's arteritis with good short term results.

Takayasu's arteritis is a chronic and progressive disease of unknown aetiology, commonly involving the aorta, its major branches and the pulmonary arteries (Hachiya, 1970; Das et al, 1982; Yamato et al, 1986). It frequently results in stenosing and obstructive lesions in the involved blood vessels, and dilatation and aneurysmal lesions are uncommon (Liu, 1985; Yamato et al, 1986). In view of the widespread, diffuse arterial involvement and the underlying chronic, non-specific inflammation, reconstructive vascular surgery in these patients carries a significant risk with a high incidence of graft occlusion (Hodgkins & Dutton, 1982).

Percutaneous transluminal angioplasty (PTA) has provided an attractive alternative for treating these patients. Even though the short and long term results of PTA in atherosclerosis and fibromuscular hyperplasia have been widely reported (Krepel et al, 1985; Kachel et al, 1987; Billstrom et al, 1988; Brown et al, 1988; Van Andel et al, 1988; Klinge et al, 1989; Odurny et al, 1989), the use of PTA in Takayasu's arteritis has not received adequate attention (Saddekni et al, 1980; Cook et al, 1986; Gu et al, 1988; Staller & Maleki, 1989). We have performed PTA for abdominal aortic, renal and iliac arterial stenoses in 11 patients with Takayasu's arteritis. The technical problems and initial results of PTA form the subject of this paper.

Material and methods

During the last 16 months, 11 patients with Takayasu's arteritis (six males; age range from 10 to 28 years; mean age 17.9 years) underwent PTA following initial diagnostic digital subtraction panaortoarteriography using an Angiotron CMP Unit (Siemens). The diagnosis of Takayasu's arteritis in each patient was based on the clinical, laboratory and arteriographic findings as established by the Aortitis Syndrome Research Committee of Japan (Inada et al, 1976). Erythrocyte sedimentation rate (ESR) was measured in all the patients and if raised was considered suggestive of "active" disease; PTA was performed when the disease was considered "stable" after estimating ESR. No pathologic confirmation of the diagnosis of Takayasu's arteritis could be obtained in any patient.

All the patients were considered for an initial intravenous digital subtraction angiogram (IV-DSA). Those found unsuitable or in whom IV-DSA examination was suboptimal underwent an intra-arterial DSA (IA-DSA). Intravenous DSA was performed on an outpatient basis with centrally delivered, small-volume, bolus injections of an ionic, water-soluble contrast medium (Urografin 370, Schering AG). Intra-arterial examination was performed by the percutaneous transfemoral route with a 5 French catheter and small amounts of diluted Urografin 370 (one in one dilution for aorta, and one in two dilution for medium-sized vessels). We followed a previously reported examination protocol for the evaluation of these patients (Sharma et al, 1989).

Angioplasty procedure

Patient selection

(i) Renal artery stenosis: based on the clinical and arteriographic findings, patients with 70% or more luminal diameter narrowing in the renal artery in the presence of systemic hypertension uncontrolled with drugs or needing multiple drugs for adequate control were selected for percutaneous transluminal renal angioplasty (PTRA). Nine patients underwent PTRA for 12 renal arterial stenoses (five males; age range from 10 to 28 years; mean age 19.2 years). Renal artery stenosis was unilateral in four patients. Both the renal arteries were involved in the remaining five patients; two patients had an occluded renal artery on one side and three patients showed bilateral renal artery stenosis. Percutaneous transluminal renal angioplasty was performed for bilateral renal artery stenosis in two separate procedures in two of these three patients and PTRA for the opposite kidney in the third patient is planned.

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(ii) Abdominal aortic stenosis: two patients with symptomatic short segment, 50% or more luminal diameter narrowing involving the infrarenal segment of the abdominal aorta underwent transluminal angioplasty. Both the lesions were discrete and centrally located.

Preparation

Prior to PTRA, anti-hypertensive drugs were stopped on the day before the procedure to avoid hypotension following successful dilatation. All patients undergoing PTA were started on oral Aspirin (330 mg daily) and Dipyridamole (150 mg daily) 3 days before PTA and continued for 6 months afterwards.

The procedure

Transluminal angioplasty was performed by a percutaneous transfemoral route. A control abdominal aortogram was first obtained. Subsequently for abdominal aortic PTA, the diagnostic catheter was exchanged for an appropriately sized single balloon catheter (Medi-Tech Inc, USA) by the standard exchange technique after obtaining a trans-stenotic pressure gradient. The balloon was placed across the stenosis and inflated to six atmospheres for 10 s after the "waist" had disappeared. This was followed by post-procedure pressure measurements and a diagnostic aortogram to assess the adequacy of PTA. The patients received 5000 IU heparin prior to PTA and were subsequently heparinized for 24 h (5000 IU 6 hourly intravenously). Percutaneous transluminal angioplasty was considered successful if the aortic luminal diameter was normal or improved by 50% with less than 30% residual narrowing, the pressure gradient had disappeared or was less than 20 mmHg, and the arterial collaterals had disappeared.

For PTRA, the diseased renal artery was engaged by 5 French A-2 femoral-visceral catheter (Cordis Corp, USA) and trans-stenotic pressure gradient was measured. Angioplasty was performed if the initial pressure gradient was more than 20 mmHg. After a bolus intra-arterial injection of 5000 IU of heparin, the A-2 femoral-visceral catheter was replaced by an appropriately sized balloon catheter (Medi-Tech Inc, USA) by using a 260 cm long and 0.035 inch wide exchange guidewire (USCI International). Care was taken not to use oversized balloon catheters. We frequently encountered difficulty in crossing the stenosis with the balloon catheter, and we had to use tough Teflon catheters frequently to bougie the stenotic lesion (in eight out of 10 successful PTRAs) before the balloon catheter would cross the stenosis.

Inflation was performed by hand utilizing a 10 ml syringe filled with 30% Urografin 370. The first inflation for 30 s did not result in the disappearance of the "waist" in any stenosis. The "waist" disappeared during the second inflation in six stenoses, in the third inflation in two instances, and did not completely disappear even after five dilatations in the remaining two successful PTRA studies. The balloon showed an indentation on its outer surface corresponding to the site of "waist" upon withdrawal in all but two instances (the balloon burst during the final inflation in these two instances). All the patients complained of backache during inflation of the balloon. The balloon was inflated for 10 s after disappearance of the "waist".

Immediate post-procedure pressure measurements and diagnostic aortograms were obtained in all the patients in order to assess the adequacy of angioplasty. The systemic blood pressure was carefully monitored in the subsequent 24 h and anti-hypertensive drugs were withheld during this period. Transluminal angioplasty was considered as clinically rewarding if the blood pressure became normal or if the diastolic pressure had decreased by 10 mmHg following the procedure. The result of PTRA was interpreted as a "cure" if the blood pressure remained normal after the procedure without any anti-hypertensive drugs; "improved" if there was at least 50% reduction in the amount of anti-hypertensive drugs needed to control the blood pressure following PTRA; and "failed" if PTRA resulted in no change in the pre-procedure blood pressure and drug requirement.

Follow-up evaluations were done at 24 h, 1 week, 6 weeks and then every 6 months by blood pressure and medication evaluation and by measuring walking distance, peripheral pulses and ankle–arm pressure index in the patients who underwent PTA for abdominal aortic stenosis.

Results

Nine patients underwent initial IV-DSA, all diagnostic. The remaining two patients had congestive cardiac failure and hence underwent an elective initial IA-DSA. The angiographic findings are summarized in Table I. A total of 15 angioplasties were performed in 11 patients (Table II).

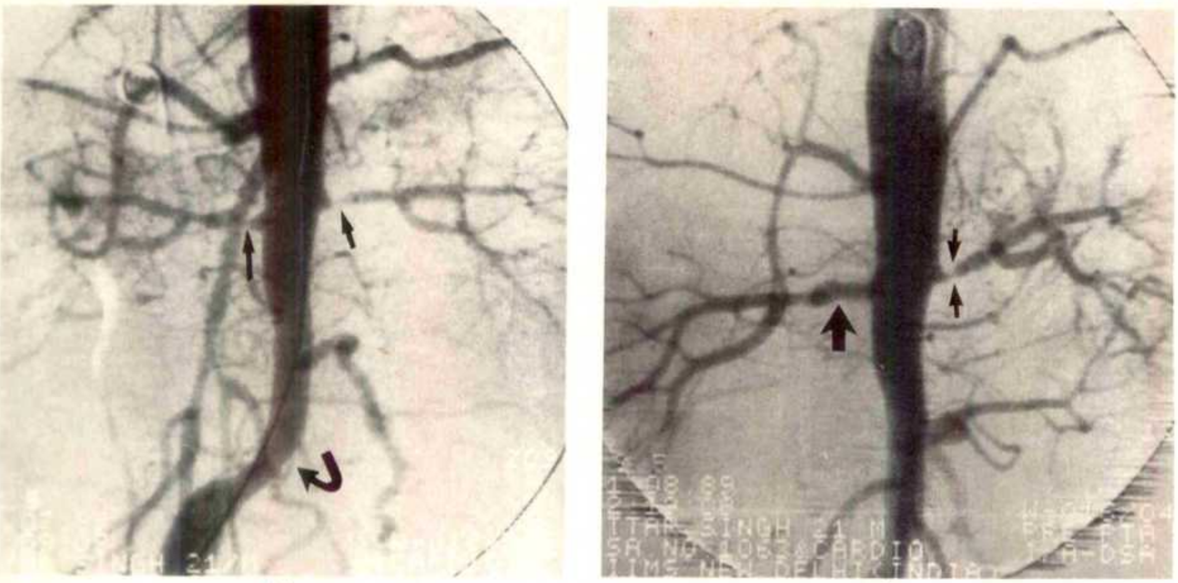
Seven patients underwent PTRA for unilateral renal

Table I. Systemic arterial abnormalities in the patients who underwent transluminal angioplasty ($n = 11$)

Vessel involved	Number of patients
Abdominal aorta	8
Aortic arch	1
Thoracic aorta	1
Renal arteries—unilateral	4
—bilateral	5
Left subclavian artery	7
Left carotid artery	1
Left iliac artery	1
Inferior mesenteric artery	1

Table II. Results of transluminal angioplasty in Takayasu's arteritis

Case number	Age	Sex	Angiographic location of lesion	Pressure gradient		Blood pressure		Angiography diameter stenosis (%)		Follow-up period	Present status
				Before	After	Before	After	Before	After		
1	16	M	Eccentric proximal right renal artery stenosis (RAS)	110	14	200/120	140/90	90	20	7 months	Restenosis after 5½ months, repeat PTRA done 1 month ago Present blood pressure 130/80
			Repeat PTRA for restenosis	110	0	180/120	130/80	90	0		
2	24	M	Proximal bilateral RAS and occluded left iliac artery	130 (Right)	10	210/130	140/100	90	0	4 months	Blood pressure 140/100 Left lower limb pulses well felt and no claudication
				110 (Left)	14			80	0		
3	12	M	3 cm long stenosis of infrarenal segment of abdominal aorta	40	10	180/120	130/90	80	10	9 months	Blood pressure 120/80
4	18	F	Eccentric proximal left RAS	76	12	170/110	130/90	90	30	Lost from follow-up	
5	28	M	Left RAS just after its origin	Unsuccessful		180/120	180/120	90	Not crossed		
6	14	M	Localized eccentric RAS just after origin	Unsuccessful		160/110	170/110	90	Not crossed		
7	23	F	Localized stenosis of infrarenal segment of aorta	32	6	Normotensive		90	20	16 months	No narrowing or pressure gradient at 1 year follow-up study
8	15	F	Eccentric proximal right RAS	100	15	180/110	140/90	90	0	6 months	130/86
9	26	F	Eccentric proximal right RAS	84	10	190/120	150/100	80	0	Lost from follow-up	
10	10	M	Bilateral proximal eccentric RAS	76 (Right)	0	170/110	140/100	90	0	6 months	120/80
				60 (Left)	0	140/100	120/80	90	0	1 month	
11	22	F	Eccentric proximal right RAS	Not measured		180/110	150/110	80	30	1 month	150/100



(a) (b)

Figure 1. (a) Intra-arterial DSA of the abdominal aorta in the antero-posterior view showing tight, proximal narrowings of both renal arteries (arrow) and complete occlusion of left common iliac artery (curved arrow). (b) Abdominal aortogram after angioplasty. The arterial lumen has become normal. Note that the arterial catheter has now been placed across the left iliac artery. This was also subsequently dilated.

artery stenosis. In addition, one of these patients underwent repeat PTRA for restenosis 6 months after the initial procedure. Two patients underwent PTRA for bilateral renal artery stenosis (Fig. 1). Initial haemodynamic and angiographic success as shown by post-PTRA pressure measurements and angiography was obtained in 10 lesions in seven patients. There were two technical failures owing to the inability to cross the lesion. In one of these patients, the lesion was crossed with a hi-torque Flex-T™ guidewire (ACS, Inc, USA) but the balloon catheter would not cross the stenosis and the procedure was abandoned. The renal artery stenosis could not be crossed even by the guidewire in the second patient. The mean diastolic blood pressure before PTRA was 115.8 mmHg and immediately after PTRA was 96.6 mmHg. Except in one patient (Case 11), all the remaining patients showed an immediate fall in the diastolic blood pressure following PTRA. The diastolic blood pressure showed a further fall during the follow-up period.

Two patients were lost to follow-up. In the remaining five patients (eight lesions), the follow-up period ranged between 1 and 8 months (mean, 5 months). Restenosis was documented in one patient who underwent PTRA for right sided renal artery stenosis. He was normotensive for 5½ months after PTRA when he again developed hypertension (Case 1). Intravenous DSA showed restenosis at the previous PTRA site. A repeat successful PTRA was performed and he is normotensive 1 month after repeat angioplasty. PTRA resulted in a "cure" for hypertension in four patients, improvement in hypertension in three patients, and "failed" in two patients.

Two patients underwent PTA for localized, discrete, abdominal aortic stenoses involving the infrarenal segment. Both the patients showed immediate haemodynamic and angiographic improvement following PTA. Both these patients also complained of backache during inflation of the balloon. Repeat catheterization and angiography at 6 months (Fig. 2) in one patient (total follow-up 9 months) and at 12 months in the other patient (total follow-up 16 months) showed no residual stenosis or no significant pressure gradient at the PTA site (mean follow-up 12.5 months).

Discussion

Percutaneous transluminal angioplasty is a viable alternative to reconstructive surgery in the management of atherosclerosis and fibromuscular hyperplasia with good short and long term results (Krepel et al, 1985; Brown et al, 1987; Billstrom et al, 1988; Van Andel et al, 1988; Klinge et al, 1989; Odurny et al, 1989). Saddekni et al (1980) first reported successful PTRA in a patient with Takayasu's arteritis with renovascular hypertension. Subsequently, Hodgkins and Dutton (1982) performed successful PTA for subclavian and carotid arterial stenoses in a patient with Takayasu's arteritis; since then, PTA has been tried in the management of renal, abdominal and thoracic aortic stenoses in a few patients with encouraging initial results (Hiramatsu et al, 1983; Liu, 1985; Gu et al, 1988; Khalilullah et al, 1988). Our early results compare favourably with those reported in the literature (Table III).

Even though the use of PTA in the management of Takayasu's arteritis has been occasionally reported, no

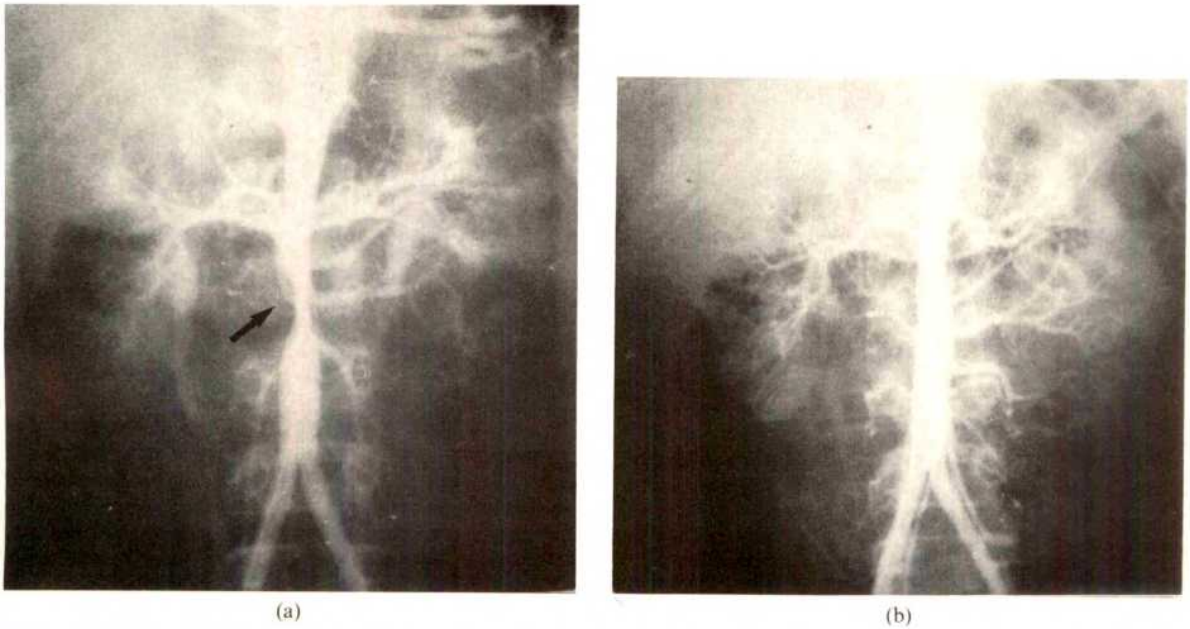

(a) (b)

Figure 2. (a) Abdominal aortogram in the antero-posterior view showing tight narrowing of the infrarenal segment of abdominal aorta and mild stenosis of both renal arteries (arrow at abdominal aortic stenosis). (b) Abdominal aortogram after angioplasty showing only mild residual narrowing. The patient's blood pressure became normal after angioplasty.

specific problems associated with PTA in this clinical setting have been previously described. We have often found that, whereas the guidewire would easily cross the stenosis in these patients, it was difficult to place a balloon catheter across the lesion. In addition, the patients often complained of back pain during inflation of the balloon for abdominal aortic or renal angioplasty, even though we do not use balloon catheters whose diameter exceeds the luminal diameter of the pre-stenotic segment of the involved blood vessel. It has also been noticed that these stenoses resist dilatation for longer periods and we frequently had to inflate the balloons two to three times for as long as 45–60 s before the "waist" would disappear. After withdrawing the balloon catheter, we often noticed an indentation on the outer surface of the balloon corresponding to the site of

Table III. Previous reports of percutaneous transluminal angioplasty in Takayasu's arteritis

Series	Number of patients	Vessel dilated	Result
Saddekni et al, 1980	1	Renal	Successful
Hodgkins & Dutton, 1982	1	Subclavian and carotid arteries	Successful
Hiramatsu et al, 1983	5	Renal artery	Initial success in all but recurrence in three patients within 6 months
Liu, 1985	5	Renal artery	Initial success in all
Cook et al, 1986	1	Renal artery	Successful
Dong et al, 1987	22	Renal artery	86.4% cured or improved at 6 months
Khalilullah et al, 1988	4	Descending thoracic and abdominal aorta	Successful in all
Gu et al, 1988	9	Abdominal aorta	Follow-up in seven patients; all free of symptoms
Staller & Maleki, 1989	1	Innominate and left subclavian arteries	Successful
Total	49		

the stenosis. We have rarely encountered these problems during PTA for atheroslcerotic lesions.

These observations may be related to the non-compliant nature of the vessel wall in Takayasu's arteritis, which is characterized by chronic, non-specific inflammation of the vessel wall resulting in extensive fibrosis, thickening and adhesions. In view of the underlying pathogenesis, one should avoid using oversized balloon catheters in order to avoid rupture of the rigid vessel wall. Besides, the long term patency rate and incidence of restenosis after initial successful dilatation using stronger and more prolonged trauma to the intima of the vessel wall will be interesting. Hiramatsu et al (1983) performed PTRA in five patients, with initial success in all of them but there was recurrence of the lesion in three patients within 6 months. The authors believed the unsatisfactory follow-up result might have been either because of the progressive character of this disease or because the dilatation effect may just have been temporary in a rigid stenosis. It appears that PTA in Takayasu's arteritis is best performed in "stable" arterial stenoses. The erythrocyte sedimentation rate should be estimated and angioplasty avoided during the "active" stage of the disease.

At present, we are unable to comment on the long term patency rates of PTA in this disease. The initial results have been very encouraging. Restenosis was observed in only one renal artery stenosis which was successfully redilated. Percutaneous transluminal angioplasty offers an attractive alternative to reconstructive vascular surgery.

References

Billstrom, A., Ekelund, L. & Hietala, S. O., 1988. Complications of percutaneous transluminal renal angioplasty. *Journal of Interventional Radiology, 3*, 45–51.

Brown, K. T., Schoenberg, N. Y., Moore, E. D. & Saddekni, S., 1988. Percutaneous transluminal angioplasty of infrapopliteal vessels: Preliminary results and technical considerations. *Radiology, 169*, 75–78.

Cook, P. G., Wells, I. P. & Marshall, A. J., 1986. Renovascular hypertension in Takayasu's disease treated by percutaneous transluminal angioplasty. *Clinical Radiology, 37*, 583–584.

Das, J. P., Padhee, B., Mishra, M., Basit, M. A., Nayak, C. R. & Swain, V., 1982. Non-specific aorto-arteritis. *Indian Heart Journal, 34*, 391–395.

Dong, S. J., Li, S. & Lu, X., 1987. Percutaneous transluminal angioplasty for renovascular hypertension in arteritis: Experience in China. *Radiology, 162*, 477–479.

Gu, S. M., Lin, G., Yi, R., Li, J. M., Zhou, J. & Pan, W. M., 1988. Transluminal catheter angioplasty of abdominal aorta in Takayasu's arteritis. *Acta Radiologica (Diagnosis), 29*, 509–513.

Hachiya, J., 1970. Current concepts of Takayasu's arteritis. *Seminars in Roentgenology, 5*, 245–259.

Hiramatsu, K., Iwata, Y., Kohda, E., Narimatsu, Y. & Hisa, S., 1983. Percutaneous transluminal renal angioplasty in Takayasu's arteritis. *International Angiology, 2*, 69–73.

Hodgkins, G. N. & Dutton, J. W., 1982. Subclavian and carotid angioplasties for Takayasu's arteritis. *Journal of Canadian Association of Radiologists, 33*, 205–207.

Inada, K., Swashima, Y., Okada, A. & Shimizu, Y., 1976. Aortitis syndrome: the diagnostic criteria. *Gendai-Iryo, 8*, 1183–1188.

Kachel, R., Endert, G., Basche, S., Grossmann, K. & Glaser, F. H., 1987. Percutaneous transluminal angioplasty (dilatation) of carotid, vertebral and innominate artery stenosis. *Cardiovascular and Interventional Radiology, 10*, 142–146.

Khalilullah, M., Tyagi, S., Lochan, R., Yadav, B. S., Nair, M., Gambhir, D. S. & Khanna, S. K., 1988. Percutaneous transluminal balloon angioplasty of the aorta in patients with aortitis. *Circulation, 76*, 597–600.

Klinge, J., Mali, W. P. T. M., Puijlaert, C. B. A. J., Geyskes, G. G. G., Becking, W. B. & Feldberg, M. A. M., 1989. Percutaneous transluminal renal angioplasty: Initial and long term results. *Radiology, 171*, 501–506.

Krepel, V. M., Van Andel, G. J., Van Erp, W. F. M. & Breslau, P. J., 1985. Percutaneous transluminal angioplasty of the femoropopliteal artery: Initial and long term results. *Radiology, 156*, 325–328.

Liu, Y. Q., 1985. Radiology of aorto-arteritis. *Radiology Clinics of North America, 23*, 671–688.

Odurny, A., Colapinto, R. F., Sniderman, K. W. & Johnston, K. W., 1989. Percutaneous transluminal angioplasty of abdominal aortic stenosis. *Cardiovascular and Interventional Radiology, 12*, 1–6.

Saddekni, S., Sniderman, K. W., Hilton, S. & Sos, T. A., 1980. Percutaneous transluminal angioplasty in non-atherosclerotic lesions. *American Journal of Roentgenology, 135*, 975–982.

Sharma, S., Aggarwal, S., Talwar, K. K. & Rajani, M., 1989. Intravenous digital subtraction angiography in non-specific aorto-arteritis. *British Journal of Radiology, 62*, 117–120.

Staller, B. J. & Maleki, M., 1989. Percutaneous transluminal angioplasty for innominate artery stenosis and total occlusion of subclavian artery in Takayasu's type arteritis. *Catheterization and Cardiovascular Diagnosis, 16*, 91–94.

Van Andel, G. J., Van Erp, W. F. M., Krepel, V. M. & Breslau, P. J., 1988. Percutaneous transluminal dilatation of the iliac artery: long term results. *Radiology, 156*, 321–323.

Yamato, M., Lecky, J. W., Hiramatsu, K. & Kohda, E., 1986. Takayasu's arteritis: radiographic and angiographic findings in 59 patients. *Radiology, 161*, 329–334.

1990, *The British Journal of Radiology*, *63*, 523–531

Evaluation of response to chemotherapy of human cystic echinococcosis

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Abstract. Fifty-five patients with echinococcosis were treated with mebendazole (30) and albendazole (25). To determine changes in cyst morphology and to evaluate the varying degree of response, progress during follow-up was shown by radiography, computerized tomography and ultrasonography. Persistence of cysts without any change in the morphology and cyst enlargement were taken as criteria for unsuccessful treatment. Development of echogenic foci and increase in density of cyst fluid were considered as a therapeutic effect. Changes in cyst wall such as thickening and deposition of calcium and detachment of the cyst membrane may also indicate response. An essential criterion, for a positive drug effect, was cyst size reduction as well as shape deformation. However, the most convincing and reliable criterion was the complete disappearance of hydatid cysts. Comparative assessment of the therapeutic effect of the two drugs favoured albendazole.

Conventional diagnostic procedures used in human cystic echinococcosis have included a number of serological methods (Kagan, 1968; Hess et al, 1974; Eckert & Wissler, 1978; Rickard, 1979; Todorov, 1980), chest radiographs, plain films of upper abdomen (Bonakdarpour, 1967; Morris et al, 1967), contrast media studies of the gastrointestinal and hepatobiliary tract (Saidi, 1976), radioisotope liver scanning (Czerniak et al, 1964; Garrett et al, 1976) and angiography (McNulty, 1968; Baltaxe & Flemming, 1970).

With the introduction of ultrasonography (Babcock et al, 1978; Spiegel et al, 1978; Gharbi et al, 1981; Niron & Özer, 1981) and computerized tomography (Kirschner et al, 1978; Scherer et al, 1978; Alltree, 1979; Beggs, 1983) newer methods have become available for detection of hydatid disease.

Changes in appearance of the cysts during treatment are not well known and they remain ill defined (Morris et al, 1984; Bekhti & Nizet, 1986).

The purpose of our study was to use non-invasive methods for diagnosis and follow-up of patients with hydatid disease treated with mebendazole and albendazole, and to determine and classify the changes in cyst morphology after chemotherapy.

Patients and methods

Fifty-five patients with echinococcosis were included in the study. Thirty of these were treated with mebendazole (16 females, 14 males, mean age 40.2 years, range 6–59 years), and 25 with albendazole (13 females, 12 males, mean age 41 years, range 10–58 years). Mebendazole was administered at a dose of 50–70 mg/kg/day continuously for between 6 and 24 months (mean of 10.3 months; mean total dose given per patient 1250 g) and albendazole in daily doses 10 mg/kg/day for four courses of 30 days with an interval of 15 days between courses (mean 5.5 months including intervals; mean total dose given per patient 84 g).

The pre-treatment diagnosis of hydatid cysts and the assessment of the changes in cyst morphology were performed at regular intervals using radiography, ultrasound and computerized tomography (CT) as appropriate. Hydatid disease was confirmed by several immunodiagnostic tests.

For assessment of evolution during follow-up, the following changes in the radiological and ultrasound images were noted:

(a) no change in cyst morphology;
(b) change in intracyst structure;
(c) change in cyst wall;
(d) cyst size reduction and deformation;
(e) cyst disappearance.

Response was classified into three groups, as follows: *success*—disappearance, decrease in size, deformation in shape and calcification in all cysts; *partial success*—the above changes in some but not in all cysts, hyperechoic appearance, increased density of cyst content; *no success*—no changes in cyst morphology.

Results

Thirty-two out of 55 patients studied had hydatid cysts in a single organ (16 in liver, eight in lung, four in bone and one in spleen, abdomen, brain and spine). In the remaining 22 patients the cyst site was in two or three organs (four in liver and lungs, seven in liver and abdomen, one in liver and spleen, one in liver and brain, six in liver, spleen and abdomen and three in liver, lungs and spleen). Cyst numbers varied considerably: 10 patients had a single cyst, 20 had 2–5 cysts, 11 had 6–10 cysts and 10 patients had over 10 cysts. Cyst size varied from 1–2 cm to 10 cm in diameter. The mean follow-up period was 28 months.

Table I. Changes in cyst morphology in patients treated with mebendazole, according to cyst site and number

Cyst site	Cyst number and patients affected	Patients treated, cyst number and changes				
		No change	Change in intracyst structure	Change in cyst wall	Size reduction	Cyst disappearance
Liver	75 (21)	26 (12)	7 (5)	2 (2)	3 (2)	37 (5)
Lungs	56 (9)	17 (5)	0 (0)	0 (0)	2 (1)	37 (5)
Spleen	9 (6)	5 (4)	0 (0)	0 (0)	0 (0)	4 (2)
Abdomen	16 (5)	4 (3)	0 (0)	0 (0)	1 (1)	11 (1)
Brain	1 (1)	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Total	157 (42)	53 (25)	7 (5)	2 (2)	6 (4)	89 (13)
Changes in cysts (%)		33.7	4.5	1.3	3.8	56.7
Patients affected (%)		51.0	10.3	4.1	8.1	26.5

Figures in brackets: number of patients affected.

The number of patients, the number of cysts examined and the changes in cyst morphology following mebendazole and albendazole treatment are presented in Tables I and II.

Since cysts at several sites were present in some patients, and cysts in one organ in a single patient may differ in response, denominators for calculating overall changes exceed the true number of patients.

The two patients with bone lesions in each treatment group have been excluded from evaluation of cyst morphology since the details and number of cysts could not be identified initially. Radiographic and CT examination did not reveal any changes in bone structure which could be connected with medical treatment. However, the clinical state of both patients treated with albendazole improved considerably.

No change in cyst morphology

Despite mebendazole treatment, no change was seen in 53 (33.7%) out of 157 cysts in varying sites and corresponding to 25 (51%) out of 49 patient cyst responses (Table I). In particular, no morphological changes in 12 patients were observed in 26 of a total of 75 liver cysts. Similar proportions of cysts without change are seen in other tissues. In three patients treated with mebendazole, an enlargement of liver cysts (two patients) and a spleen cyst (one patient) was observed (Fig. 1).

Albendazole treatment did not induce any morphological changes in 16 patients in 40 (25.0%) of 160 cysts in varying sites. In the liver, no change in morphology was observed in seven patients in 16 of 72 cysts. The number of cysts without any changes for the different localizations are given in Table II. No cyst treated with albendazole increased in size.

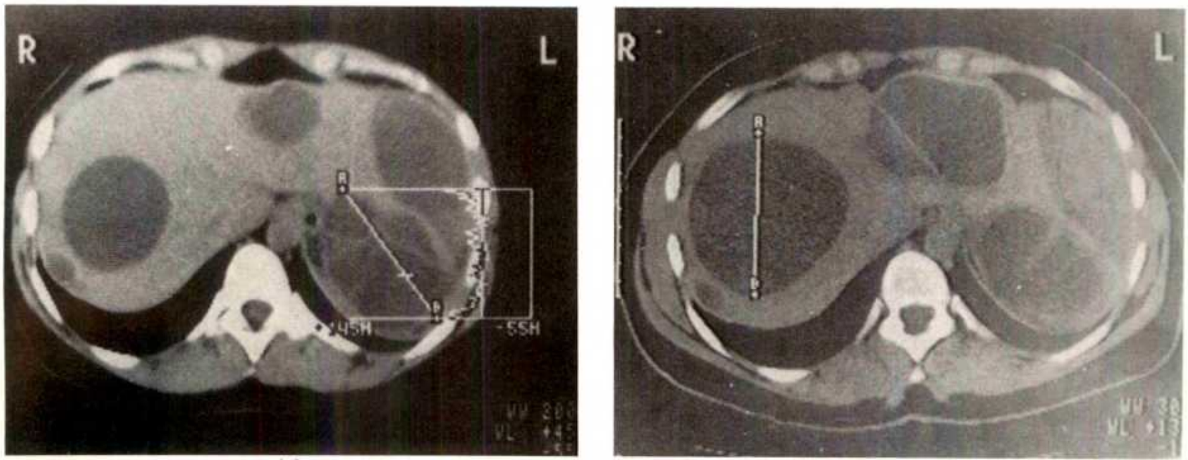
Changes in intracyst structure

After drug treatment some liver, lung, spleen and abdominal cysts underwent sonographic changes in their intracyst structure, characterized by the presence

Table II. Changes in cyst morphology in patients treated with albendazole, according to cyst site and number

Cyst site	Cyst number and patients affected	Patients treated, cyst number and changes				
		No change	Change in intracyst structure	Change in cyst wall	Size reduction	Cyst disappearance
Liver	72 (18)	16 (7)	8 (4)	3 (1)	12 (7)	33 (9)
Lungs	24 (6)	1 (1)	2 (2)	1 (1)	0 (0)	20 (5)
Spleen	9 (5)	4 (3)	3 (2)	1 (1)	0 (0)	1 (1)
Abdomen	43 (9)	18 (4)	3 (2)	0 (0)	8 (4)	14 (3)
Brain	9 (2)	1 (1)	0 (0)	0 (0)	0 (0)	8 (1)
Spine	3 (1)	0 (0)	0 (0)	0 (0)	3 (1)	0 (0)
Total	160 (41)	40 (16)	16 (10)	5 (3)	23 (12)	76 (19)
Changes in cysts (%)		25.0	10.0	3.1	14.4	47.5
Patients affected (%)		26.6	16.6	5.0	20.0	32.7

Figures in brackets: number of patients affected.

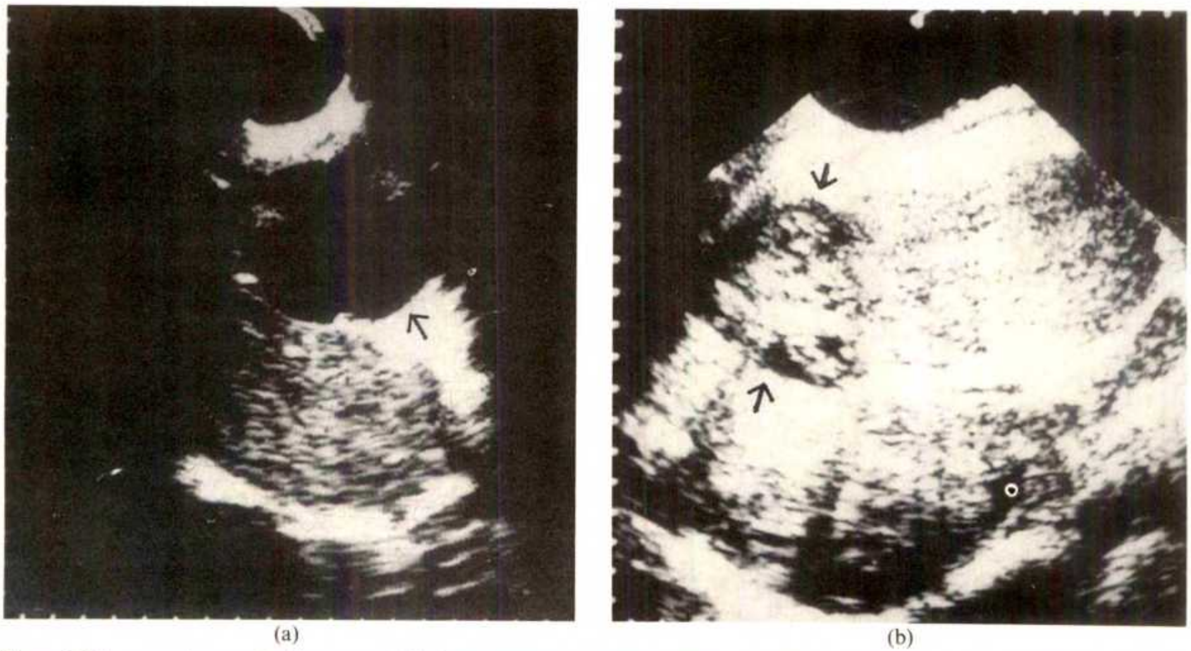


(a) (b)

Figure 1. Computerized tomography of liver: (a) hydatid cysts of liver and spleen before treatment; (b) enlargement of liver and unchanged spleen cysts 12 months after completion of therapy with mebendazole.

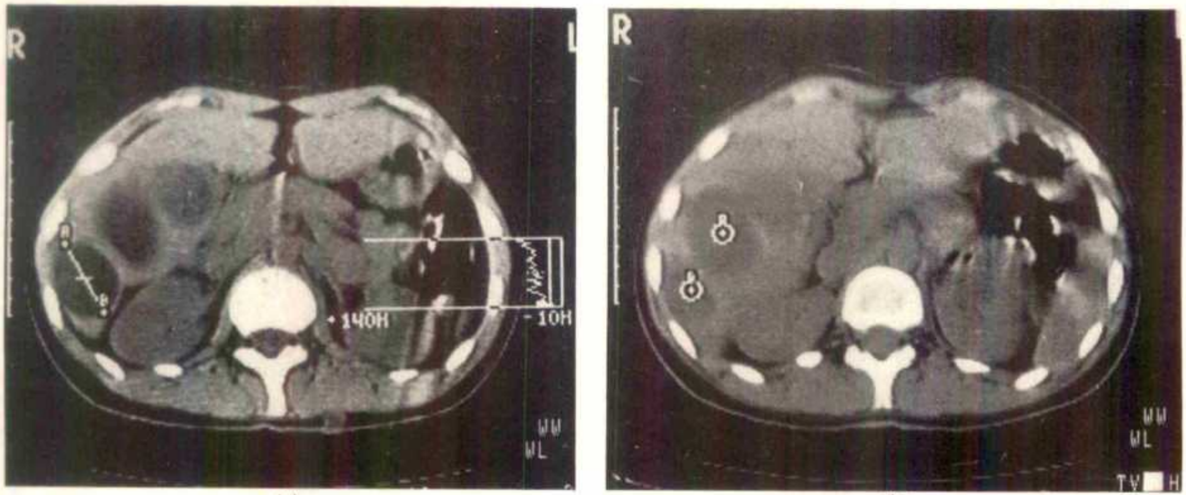
of hyperechoic areas (Fig. 2). The CT images of the cysts showed increased density of their content, in the range of 30–50 Hounsfield Units (HU) (Fig. 3). Prior to treatment, cyst density had been low: close to that of water.

In five patients treated with mebendazole, only seven (4.5%) liver cysts underwent changes in intracyst structure. The number of cysts with changes in intracyst structure after albendazole treatment was 16 (10%) seen in 10 patients. Changes were also observed in spleen, abdominal and pulmonary cysts, when examined by CT, but only in patients treated with albendazole (Tables I and II). In general, the changes in cyst structure were not frequent. In some cysts, a non-homogeneous appearance of the CT image was detected. The difference in density, measured in HU from one cyst section to another, however, was not significant. Corresponding echographic images were not diffusely echogenic, there being hyperechoic areas with foci of hypoechoic structures. In some liver cysts, daughter cysts have been



(a) (b)

Figure 2. Ultrasound scans of a liver cyst: (a) before treatment—anechoic appearance; (b) hyperechoic appearance 12 months after starting therapy with mebendazole (arrows).



(a) (b)

Figure 3. Computerized tomography of liver cysts: (a) before treatment—water-like density (12 HU); (b) increased density of cyst content 6 months after starting therapy with albendazole (36 HU).

observed producing a multivesicular appearance. These cysts did not change after therapy with either drug or during follow-up but remained anechoic and of low density (Fig. 4).

Changes in cyst wall

In five liver and spleen cysts in three patients, after a considerable period of follow-up a thickening of the fibrous capsule was observed. This occurred more often in older and larger cysts and represents 1.6% of all cysts treated. The outer contour of the cysts became very hyperechoic. In addition, calcification appeared in walls of two further cysts, one in liver, treated with mebendazole and another in spleen, treated with albendazole. There was partial calcification with thickening and high density with spots of calcification seen on CT (Fig. 5). This type of cyst wall calcification was very rare: 0.6% of all cysts treated, and occurred 20–24 months after completion of medical treatment.

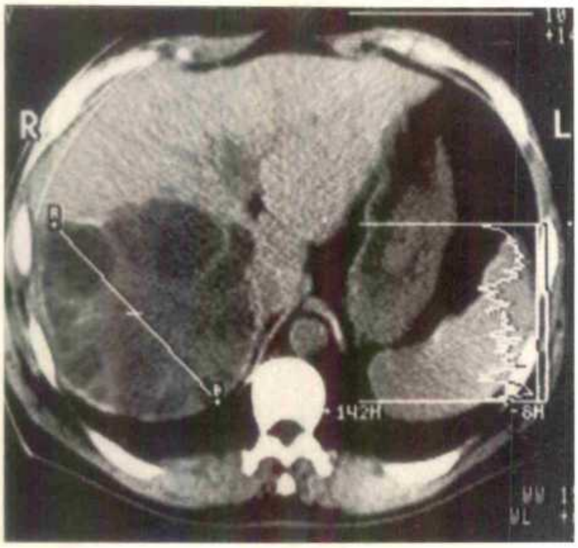


Figure 4. Computerized tomography of a liver cyst with daughter cysts, 13 cm in diameter: the density of daughter cysts was water-like (5–8 HU), while that of central cyst area is considerably higher (35 HU). The cyst appearance did not change 6 months after starting therapy with mebendazole for liver and lung cysts. At surgery, viable daughter cysts and many ruptured daughter cysts were present.

In two patients with liver and spleen cyst, detachment of the cuticular layer and germinal membrane was seen after albendazole therapy (Fig. 6).

Cyst size reduction and/or deformation

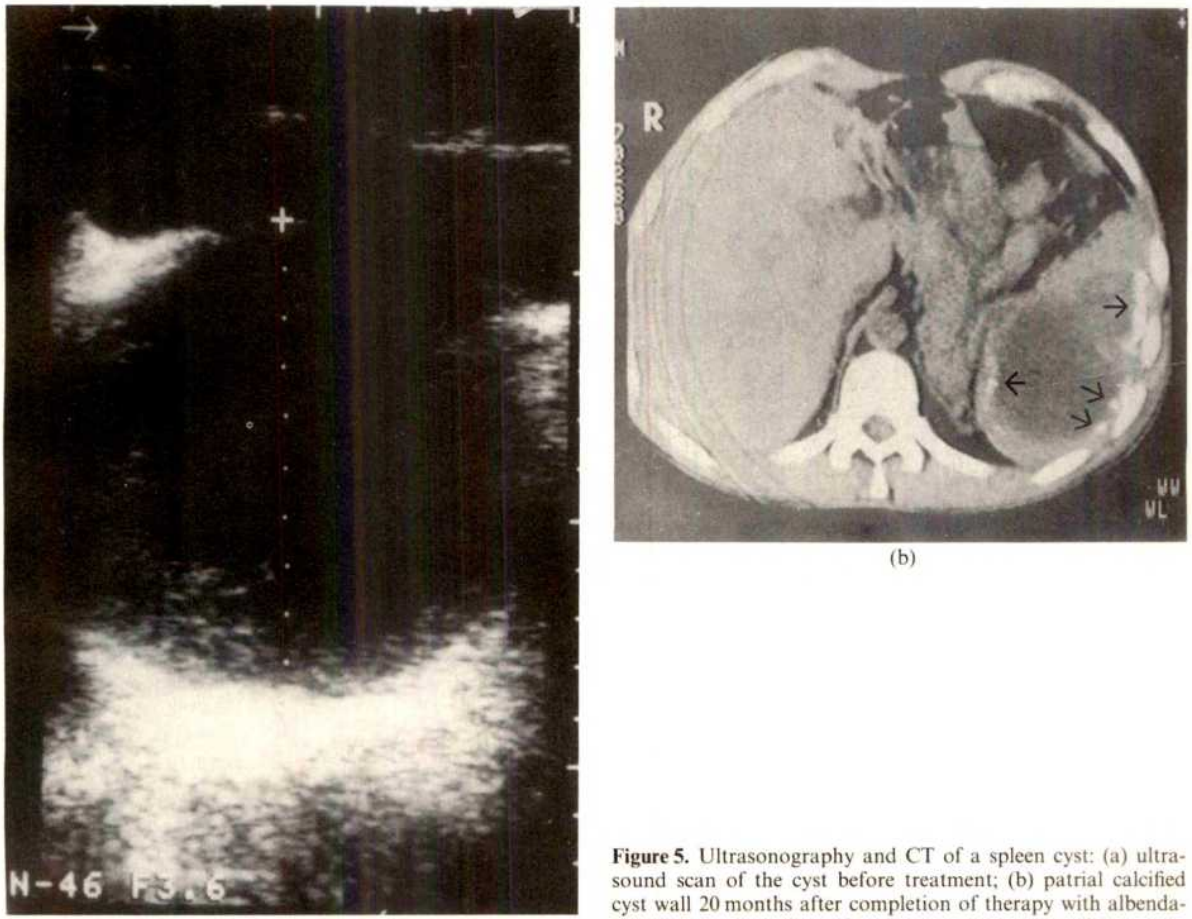
Reduction of cyst size followed by, in some cases, deformation of their shape was observed in six (3.8%) cysts treated with mebendazole and in 23 (14.4%) cysts treated with albendazole (Tables I and II). These changes were more frequent in liver and abdominal cysts than in other cysts (Fig. 7). Size reduction and deformation of treated cysts were in general associated with increased internal echoes and density.

Cyst disappearance

Some hydatid cysts in liver, lungs, spleen, abdomen and brain disappeared completely or partially. Eighty-nine (56.7%) out of 157 cysts disappeared following treatment with mebendazole, in 13 (26.5%) patients. In the cysts treated with albendazole 76 (47.5%) out of 160 cysts disappeared (Tables I and II). This effect was observed mostly in liver and lung cysts (Figs 8 and 9).

Comparative evaluation of response

In patients treated with mebendazole, successful response occurred in eight (26.6%) patients, partial



(a)

(b)

Figure 5. Ultrasonography and CT of a spleen cyst: (a) ultrasound scan of the cyst before treatment; (b) patrial calcified cyst wall 20 months after completion of therapy with albendazole. Small spots of calcificates are seen in cyst wall (arrows).

response in a further eight (26.6%) and no response in 12 (42.8%) cases. In albendazole treated patients successful response was observed in 10 (43.5%), partial response in 10 (43.5%) and no response in only three (13%) patients.

Evaluation of response in the patients with bone echinococcosis on the basis of cyst morphology is impossible, as bone structure remained unchanged. However, the clinical improvement of two patients in this group, treated with albendazole, should be taken as an indication of some response, the degree of which is difficult to determine.

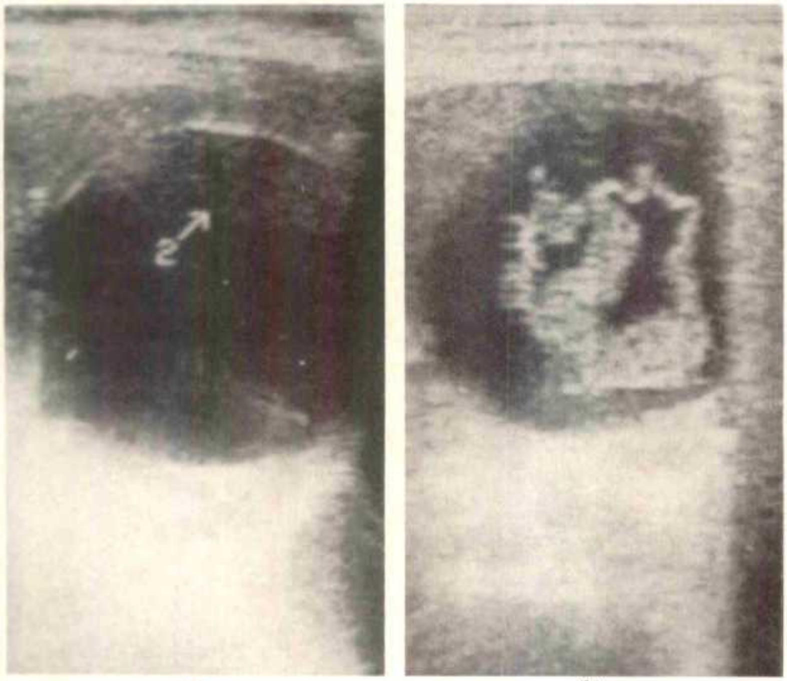
Discussion

A major problem, noted by most authors, is the lack of reliable methods for defining and measuring the therapeutic response in hydatid disease (Bryceson et al, 1982; De Rosa & Teggi, 1985). Objective criteria for evaluation of the degree of response are needed.

Examination of hydatid cysts after surgery or expectoration, together with animal inoculation of protoscolices, presents reliable methods for confirmation of the success or failure of chemotherapy, but generally this data is not available to the investigator. Continued follow-up, using non-invasive methods such as radiography, sonography and CT, is necessary to provide a morphological basis to determine the outcome of the disease (Morris et al, 1985; Bekhti & Nizet, 1986; Rudwan et al, 1986).

The pre-treatment data showed that the non-invasive methods used have a high accuracy in the diagnosis of hydatid disease, and provide precise anatomical localization and permit assessment of cyst number and size. Errors in cyst number were rare. However, they might be made in the range of ± 1–2 when the number of cysts exceeds 8–10. Both ultrasonography and CT can demonstrate calcification and daughter cysts and the latter method can determine cyst density objectively.

We have confirmed the usefulness of non-invasive methods in follow-up of cyst changes after medical treatment. As not all cysts in the same location responded equally to chemotherapy, it was essential to follow the changes in each cyst. This allowed us to evaluate the role of imaging criteria and some factors determining the degree of response.



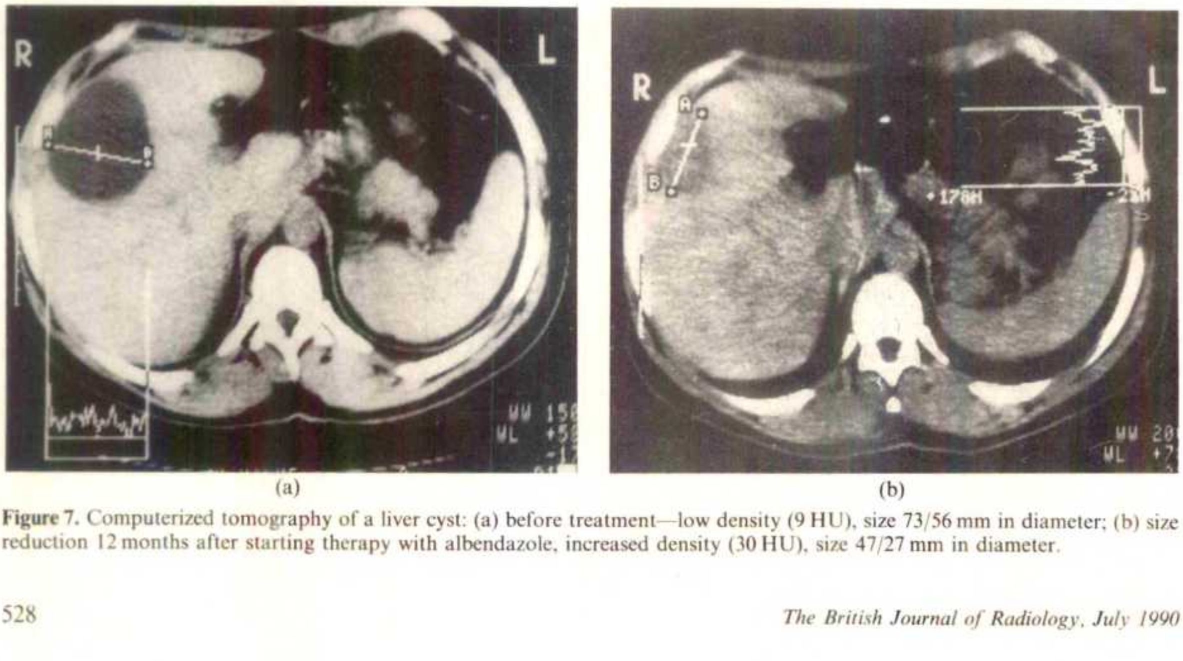
(a) (b)

Figure 6. Ultrasound scans of a spleen cyst: (a) before treatment—anechoic appearance; (b) detachment of laminated membrane 12 months after completion of therapy with albendazole.

Imaging criteria

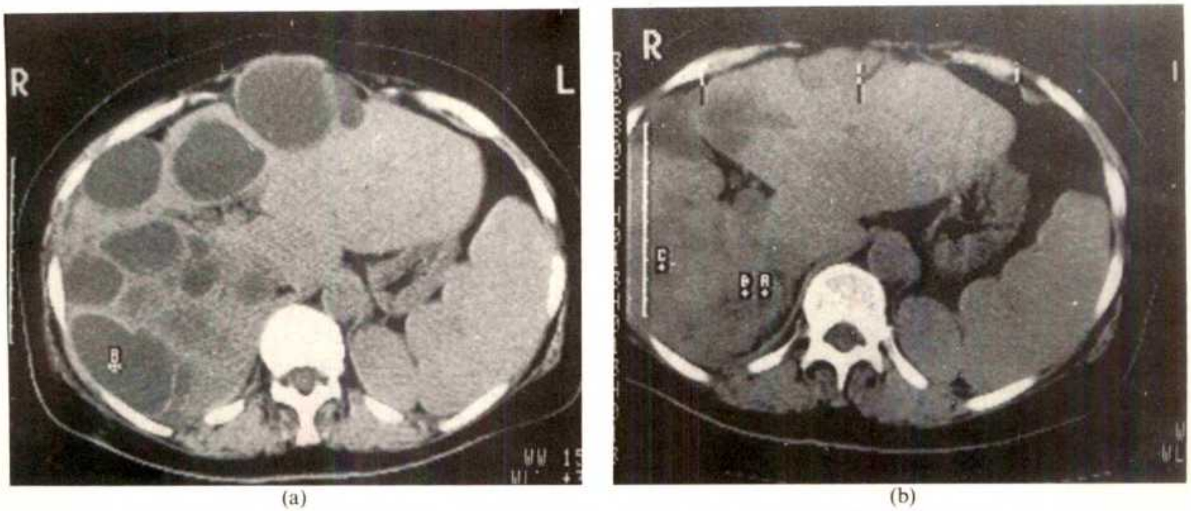
The therapeutic effect should be regarded as ineffective when, at least two years after completion of treatment, ultrasound and radiological images of the cysts remain unchanged, or an enlargement of the cysts is observed. This criterion should be interpreted cautiously in cases of bone echinococcosis, because even if the parasite has been killed the regeneration process in bones is very slow and is difficult to detect. It is also possible that some cysts in other sites are actually non-viable but, for anatomical or physiological reasons, do not show the changes indicated in our evaluation.

Transformation of an anechoic cyst to a hyperechoic appearance on ultrasound and increase of density on CT should be taken as a favourable drug effect. In some cases, however, during the follow-up, reappearance of anechoic structures with water-like density have been observed which could be classified as recurrence due to



(a) (b)

Figure 7. Computerized tomography of a liver cyst: (a) before treatment—low density (9 HU), size 73/56 mm in diameter; (b) size reduction 12 months after starting therapy with albendazole, increased density (30 HU), size 47/27 mm in diameter.



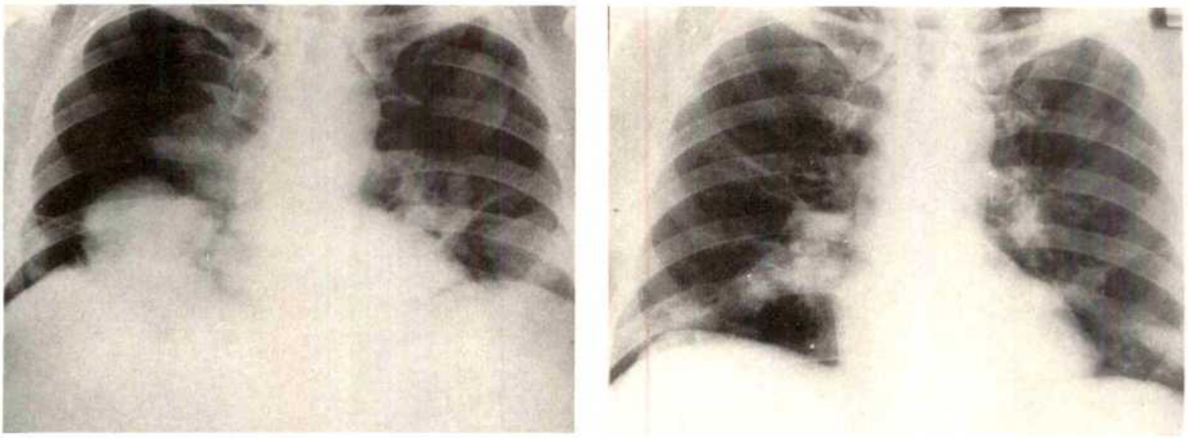
(a) (b)

Figure 8. Computerized tomography of liver cysts: (a) before treatment—many cysts in the liver; (b) disappearance of liver cysts 12 months after starting therapy with albendazole; some residual spots are seen of high density, near to that of the liver.

short treatment duration. It has also been observed in large and old cysts. We therefore feel that this appearance should be accepted as a marker of a therapy effect only after considerably longer follow-up, say for two years. However, in cases with daughter cysts within the primary cyst, and a multicystic appearance, the daughter cysts may be anechoic with water-like density, while the remaining part of the cyst may be hyperechoic with high density, from ruptured daughter cysts. This should not be considered as a favourable drug effect. After treatment in our study, daughter cysts did not disappear on ultrasound and CT as reported by some authors (Morris et al, 1985; Singeharoen et al, 1985); instead they appeared to rupture. We conclude that these cysts are very resistant to both mebendazole and albendazole and their effective treatment seems to be difficult.

Detachment of cyst membranes after treatment is most probably a result of diminished endocystic pressure, as a result of hydatid fluid resorption, reduced secretion or cyst rupture in case of pulmonary echinococcosis. Splitting of the wall, producing an undulating floating membrane, was also observed. Complete collapse of the endocyst produces an ultrasound marker described as the "water lily sign" where the endocyst floats in the ectocyst (Niron & Özer, 1981; Gharbi et al, 1982). If the detachment is accompanied by internal hyperechogenicity and high density cyst images, it is likely that drug treatment has been effective. However, even in these cases, development of daughter cysts is not excluded (Thompson, 1988).

Thickening and especially calcification of the cyst wall could be taken as a therapeutic response if their appearance has been detected during follow-up and was absent



(a) (b)

Figure 9. Radiographic scans of pulmonary cysts: (a) before treatment—cysts in lungs; (b) disappearance of cysts 16 months after starting therapy with mebendazole.

before treatment. Calcification, being the advanced stage of this type of change, appeared in brain cysts as early as the 12th month following treatment (Todorov et al, 1988), while calcification in the liver and spleen cysts only occurred after 3–4 years. Calcification has been said to imply death of the cysts and protoscolices (Gonzalez et al, 1979; Sutton, 1980) which, according to our observations, probably refers to more or less complete calcification of the cyst wall. Beggs (1983), however, found viable protoscolices in calcified cysts in three patients, but the degree of calcification is not mentioned. These findings in the cyst wall in our experience are very rare. Only progressive calcification, seen on serial ultrasound and CT examinations, should be accepted as a sign that the cysts have undergone morphological or degenerative changes and taken as a sign of successful therapy.

Size reduction and shape deformation were observed by the 12th month of follow-up, predominantly in smaller liver and abdominal cysts while changes in the spleen and lung cysts were not observed until the 18th–24th month after completion of treatment. Most of the larger cysts (over 8–10 cm in diameter) in liver and spleen, and especially those treated with mebendazole, maintained their size and shape despite the longer follow-up in these cases. However, some large abdominal and pelvic cysts treated with albendazole decreased in size and changed shape.

This response is very important for evaluation of the effect of medical treatment. However, it requires a continuous follow-up for at least 2 years. Some have questioned whether shrinkage indicates death of cysts and protoscolices (Beggs, 1983). Our observations, however, support the idea that both mebendazole and albendazole may have a lethal effect on smaller hydatid cysts, as no recurrences have been observed in cysts with this type of change.

The most important finding was the disappearance, after treatment, of hydatid cysts. This is indeed the most convincing and reliable criterion for assessing response and is an indication that the drugs used have had a lethal effect upon the hydatid parasite. Cyst disappearance has been reported by other authors (Bekhti et al, 1977; Gil-Grande et al, 1983; Morris et al, 1985) and is probably a result of complete resorption of hydatid fluid, following the destructive action of the drugs on the germinal layer. The mechanism of disappearance of pulmonary cysts is generally different. After rupture of lung cysts, the cyst fluid and membranes are expectorated, the cavity diminishes in size, fibrous tissue develops and the radiographic image disappears. This is observed more often in smaller and younger cysts without daughter cysts and calcifications.

Cyst disappearance should be regarded as the criterion with the most promising prognostic value.

Differences in response to therapy

The analysis of the data in Tables I and II suggests that albendazole is more effective than mebendazole, especially considering the percentages of cysts without changes and the proportion of patients so affected. These figures are higher for the patients treated with mebendazole (33.7 and 51.0%) than with albendazole (24.4 and 25.4%).

Further support for this conclusion is provided by cyst size reduction and deformation, the percentages for those treated with mebendazole being lower (3.8 and 8.1%) than with albendazole (14.4 and 20.3%).

The percentage of patients with disappearing cysts treated with albendazole (32.2%) is higher than for those treated with mebendazole (26.5%). On the other hand, the percentage of disappearing cysts for the patients treated with mebendazole (56.7%) is higher than for those treated with albendazole (48.1%). The former figures give some advantage to albendazole and the latter to mebendazole, largely because two patients successfully treated with mebendazole (for 24 and 10 months) had 35 cysts (in liver) and 12 cysts (in lungs), respectively.

Changes in intracyst structure and cyst wall, although rare, also indicate a better response with albendazole.

A therapeutic advantage of albendazole is also overall cyst response. The percentage of treatment success is higher for the patients treated with albendazole (43.5%), while the unsuccessful results for the same group is lower (13%) compared with the results for the patients treated with mebendazole (26.6% and 42.8%, respectively).

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References

ALLTREE, M., 1979. Scanning in hydatid disease. *Clinical Radiology, 30*, 691–697.

BABCOCK, D. S., KAUFMAN, L. & COSNOW, I., 1978. Ultrasound diagnosis of hydatid disease (Echinococcosis) in two cases. *American Journal of Roentgenology, 131*, 895–897.

BALTAXE, H. A. & FLEMMING, R. J., 1970. The angiographic appearances of hydatid disease. *Radiology, 97*, 599–604.

BEGGS, I., 1983. The radiological appearances of hydatid disease. *Clinical Radiology, 34*, 555–563.

BEKHTI, A., SCHAAPS, J.-P., CAPRON, M., DESSAINT, J.-P., SANTORO, F. & CAPRON, A., 1977. Treatment of hepatic hydatid disease with mebendazole: preliminary results in four cases. *British Medical Journal, ii*, 1047–1051.

BEKHTI, A. & NIZET, M., 1986. Radiological changes under effect of mebendazole on univesicular hydatid cysts in liver and lung. *European Journal of Radiology, 6*, 156–159.

BONAKDAZPOUR, A., 1967. Echinococcus disease. Report of 112 cases from Iran and a review of 611 cases from the United States. *American Journal of Roentgenology, 99*, 660–667.

BRYCESON, A. D. M., COWIE, A. G. A., MACLEOD, C., WHITE, S., EDWARDS, D., SMITH, J. D. & MCMANUS, D. P., 1982. Experience with mebendazole in the treatment of inoperable hydatid disease in England. *Transactions of the Royal Society of Tropical Medicine and Hygiene, 76*, 510–518.

Czerniak, P., Bank, H. & Pauzner, Y., 1964. Radioisotopic scanning in liver echinococcosis. *Radiology, 83*, 690–696.

De Rosa, F. & Teggi, A., 1985. First experience in the treatment of human hydatid disease with mebendazole. *Drugs Under Experimental and Clinical Research, XI*, 875–878.

Eckert, J. & Wissler, K., 1978. Immunodiagnose und Therapie der Echinikokkose. *Therapeutische Umschau, 35*, 760–776.

Garrett, W. J., Kossoff, G., Uren, R. F. & Carpenter, D. A., 1976. Gray scale ultrasonic investigation of focal defects on 99m Tc sulphur colloid liver scanning. *Radiology, 119*, 425–428.

Gharbi, H. A., Hassine, W., Brauner, M. W. & Dupuch, K., 1981. Ultrasound examination of the hydatic liver. *Radiology, 139*, 459–463.

Gil-Grande, L. A., Boixeda, D., Garcia-Hoz, F., Barcena, R., Lledo, A., Suarex, E., Pascasio, J. M. & Moreira, V., 1983. Treatment of liver hydatid disease with mebendazole: a prospective study of thirteen cases. *The American Journal of Gastroenterology, 78*, 584–588.

Gonzalez, L. R., Marcos, J., Illanas, M., Hernandez-Mora, M., Pena, F., Picouto, J. P., Cienfuegos, J. A. & Alvarez, J. L. R., 1979. Radiologic aspects of hepatic echinococcosis. *Radiology, 130*, 21–27.

Hess, U., Eckert, J. & Frohlich, A., 1974. Vergleich serologischer Methoden für die Diagnose der zystischen und alveolaren Echinokokkose des Menschen. *Schweizerische Medizinische Wochenschrift, 104*, 853–859.

Kagan, I. G., 1968. A review of serological tests for the diagnosis of hydatid disease. *Bulletin of World Health Organization, 39*, 25–37.

Kirschner, L. P., Ferris, R. A., Mero, J. H. & Moss, M. L., 1978. Hydatid disease of the liver evaluated by computed tomography. *Journal of Computer Assisted Tomography, 2*, 229–230.

McNulty, J. G., 1968. Angiographic manifestations of hydatid disease of the liver. *American Journal of Roentgenology, 102*, 380–383.

Morris, J., Doust, B. & Hanks, T., 1967. The roentgenologic and radioisotopic assessment of hydatid disease of the liver. *American Journal of Roentgenology, 101*, 519–542.

Morris, D. L., Skene-Smith, H., Haynes, H. & Burrows, G. O., 1984. Abdominal hydatid disease. Computed tomographic and ultrasound changes during albendazole therapy. *Clinical Radiology, 35*, 297–300.

Morris, D. L., Dykes, P. W., Marriner, S., Bogan, J., Burrows, F., Skene-Smith, H. & Clarkson, M. J., 1985. Albendazole—objective evidence of response in human hydatid disease. *The Journal of the American Medical Association, 253*, 2053–2057.

Niron, E. A. & Özer, H., 1981. Ultrasound appearances of liver hydatid disease. *British Journal of Radiology, 54*, 335–338.

Rickard, M. D., 1979. Immunological diagnosis of hydatid disease. *Australian Veterinary Journal, 55*, 99–104.

Rudwan, M. A., Mousa, A. M. & Muhtaseb, S. A., 1986. Abdominal hydatid disease: Follow-up of mebendazole therapy by CT and ultrasonography. *International Surgery, 71*, 22–26.

Saidi, F., 1976. *Surgery of Hydatid Disease* (W. B. Saunders, London), pp. 31–155.

Scherer, U., Weinzierl, M., Srurm, R., Schildberg, F. W., Zrenner, M. & Lissner, J., 1978. Computer tomography in hydatid disease of liver. *Journal of Computer Assisted Tomography, 2*, 612–617.

Singcharoen, T., Machanonda, N., Powell, L. W. & Baddeley, H., 1985. Sonographic changes of hydatid cyst of the liver after treatment with mebendazole and albendazole. *British Journal of Radiology, 58*, 905–907.

Spiegel, R. M., King, D. L. & Green, W. M., 1978. Ultrasonography of primary cyst of liver. *American Journal of Roentgenology, 131*, 235–238.

Sutton, D., 1980. *A Textbook of Radiology and Imaging* (Churchill Livingstone, Edinburgh) p. 805.

Thompson, R. C. A., 1988. *Personal communication.*

Todorov, T., 1980. *Tumoral Immune Response in Echinococcosis* (Wiss DSc, Sofia, Bulgaria).

Todorov, T., Vutova, K., Petkov, D. & Balkanski, G., 1988. Albendazole treatment of multiple cerebral hydatid cysts: case report. *Transactions of the Royal Society of Tropical Medicine and Hygiene, 82*, 150–152.

1990, *The British Journal of Radiology*, *63*, 532–534

Bacterial contamination of contrast media stored after opening

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Abstract. A barium suspension, iohexol, iopamidol and ioxaglate which were diluted with tapwater and 0.9% NaCl and dextrose saline (4% and 0.18%) were made into aliquots of 10 ml and stored at 4°C, room temperature and 37°C for 8 weeks. Regular handling and bacterial cultures were performed. These studies confirmed that environmental organisms do contaminate these solutions and that they also support viable organisms, but do not become significantly colonized at room temperature or 4°C. The solutions should be stored at room temperature or at 4°C. The diluted barium solution was the contrast medium least contaminated and if it is not contra-indicated for other reasons should be used in preference to low osmolality water soluble contrast media on the basis of its cost, radiological contrast and low microbial contamination rate.

Low osmolality water soluble (LOWS) contrast media have been shown to be suitable for gastro-intestinal studies in animals (Ginai, 1985), adults (Bell et al, 1987) and children and infants (Ratcliffe, 1986; Cohen, 1987). The expense of LOWS media prohibits their general use in gastro-intestinal radiology but there are certain clinical conditions in which their use is desirable.

One practical way of reducing the cost of LOWS media for this purpose is to use medium left over from other investigations. The patient in whom it is necessary to use LOWS media in the gastro-intestinal tract may be at risk if contrast medium which is seriously contaminated with bacteria is used. This paper reports an experiment to identify the organisms which contaminate opened contrast media bottles which were stored and handled in a non-sterile manner to determine whether significant colonization occurs.

Materials and methods

Three LOWS contrast media, one barium suspension and two solutions for intravenous infusion were tested. They were iohexol (Omnipaque 300, Sterling Pharmaceuticals), iopamirlol (Iopamiro 300, Schering Ltd), ioxaglate (Hexabrix 32, May and Baker), a barium suspension (Tixobar, Astra Pharmaceuticals), normal saline (0.9% NaCl, Travenol) and dextrose saline (4% dextrose and 0.18% NaCl, Travenol).

Testing was performed at three different temperatures in the departmental refrigerator (0–4°C), at room temperature (15–22°C) and in the departmental contrast medium warming oven (37°C) over a period of 8 weeks.

The contrast media were diluted to concentrations commonly used in paediatric radiology using tapwater as set out in Table I to a volume of 300 ml for each test liquid. Thirty millilitres of each liquid were separated into three 10 ml aliquots (one aliquot in each temperature environment) and put into sealed sterile containers which remained unopened for the 8 weeks. A further 30 ml of each liquid were divided into 10 ml aliquots and placed in sterile containers and sent immediately to the laboratory.

The remaining 240 ml of each test liquid were divided into three 80 ml aliquots and placed in clean unused standard pharmacy bottles made of clear glass with plastic screw tops and each stored in the three temperature environments for 8 weeks.

Every 7 days each of the 18 bottles was shaken, inspected and opened and 10 ml of the test liquid were removed with a syringe and aspirating cannula unique for each liquid and placed in a sterile container and sent to the laboratory. All the manipulations were done by one of the group (D.L.) and, in order to mimic the practice in radiology departments, no anti-bacterial precautions were taken. Hands were not washed and no mask was worn. The syringes and aspirating cannulae were stored in a clean and non-sterile area.

Table I. Solutions under study

4% Dextrose + 0.18% NaCl	Undiluted	300 ml
0.9% NaCl	Undiluted	300 ml
75 ml of Tixobar 100% w/v	+ 225 ml of tapwater	= 300 ml
150 ml of Iohexol 300 mg I/ml	+ 150 ml of tapwater	= 300 ml
150 ml of Iopamidol 300 mg I/ml	+ 150 ml of tapwater	= 300 ml
150 ml of Hexabrix 300 mg/ul	+ 150 ml of tapwater	= 300 ml

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All the samples sent to the laboratory were labelled in a code known only to the operator (D.L.). In the laboratory each 10 ml aliquot was inspected and mixed with 10 ml of tryptone soy broth and incubated at 35°C for 3 weeks. Direct plating of samples on receipt in the laboratory was not performed because all the solutions were crystal clear and there was insufficient sample to direct plate filter and culture in broth.

The samples were inspected daily and if they became cloudy a gram stain was performed on the cloudy sample which was subcultured onto blood agar (5% horse blood) and MacConkey agar which were incubated at 35°C in air for 48 h and examined for bacterial growth. All organisms were identified using standard methods (Lennette et al, 1985) including the A.P.I. system (Vercieu, France).

Results

Only the barium suspension became cloudy on shaking. No cloudiness or other abnormality was observed with the naked eye in any of the solutions during the course of the experiment.

Fourteen different organisms were cultured from the samples submitted to the laboratory. One-third (5/18) of the samples mixed in an unsterile manner but then sealed for 8 weeks contained organisms, whereas two-thirds of the samples in bottles opened weekly (84/144) were contaminated.

The distribution of infecting organisms is shown in Table II. The most frequently found organism was *Bacillus species* (mainly *B. cereus*). *Micrococci* were found in the liquids kept at 4°C in the refrigerator. Overall contamination rates were similar in all three temperature environments. The same organism is found more frequently in samples of different liquids taken on the same day than in samples taken from the same liquid over several weeks. This form of transmission indicates that inoculation is likely to occur during handling, rather than persisting because of colonization of the bulk of the contrast medium. The exception may be *micrococci* in iohexol at 37°C.

Discussion

Previous studies on the effect of contrast media on bacteria have been designed because of the fear that contrast media injected into or excreted into body cavities might interfere with the later microbiological diagnosis and identification of infection. Results are difficult to interpret, but in one study it was shown that conventional high osmolality contrast media tend to be antibacterial, whereas LOWS media tend to be less so (Dawson et al, 1983).

The purpose of this study was to observe which bacteria contaminate or colonize contrast media in an X-ray department if the contrast media are handled in a non-sterile manner. The need for this study was gener-

Table II. The distribution of organisms cultured from 144 samples at weekly intervals at three different temperatures

Week	1	2	3	4	5	6	7	8
Cold								
4% Dextrose				1			R	
0.9% Saline								
Tixobar	B		B		S	R	R	
Iohexol	B	B	P	B	B			B
Iopamidol	B	P	S/P		A	A	2	P
Ioxaglate	B	B	P	S	B		B	B
Room temperature								
4% Dextrose	D						S	
0.9% Saline							D	
Tixobar	B					M	S	
Iohexol	B	B	P	P	3	B	4	B
Iopamidol	M/S	M	P	P	A	A	C	M
Ioxaglate	B	B	P	P	S	B	B	5
37°C								
4% Dextrose	B					B	M/C	
0.9% Saline							M	
Tixobar	B	M		S		R	R	
Iohexol	S			B	M/D	M	M	M
Iopamidol	B	P		S	M		M	6
Ioxaglate	B	B	M	B	B	B	B	B

B = *Bacillus species* (34); P = *Pseudomonas stuzeri* (12); S = *Staphylococci epidermidis* (10); M = *Micrococcus species* (14); R = *Propionibacteria species* (5); D = *Diptheroid* (3); A = *Pseudomonas acidovorans* (4); C = *Acinetobacter calcoaceticus species* (2); 1 = *Flavobacteria species* (1); 2 = *Streptococci acremoris* (1); 3 = *Pasturella species* (1); 4 = *Pseudomonas species* (1); 5 = *Aerobic gram positive rods*; 6 = *Staphylococci aureus* (1).

ated by the expensive waste of LOWS contrast media in a paediatric X-ray department where frequently only a part of an ampoule or bottle of LOWS contrast medium is used. It has been our practice in the past to use a fresh container for each new patient and to discard any residual contrast medium at the end of each investigation. In our department it is fairly common to use LOWS media for gastro-intestinal studies in babies, infants and children and in these investigations the same degree of sterility as is required for intravascular or subarachnoid use is not required. We usually use LOWS media at dilutions almost equivalent in osmolality to plasma and therefore used the intravenous fluids (dextrose saline and normal saline) for comparison. We also used Tixobar at a 25% strength in babies in whom it is not contra-indicated. It is not our practice to use sterilized barium suspensions.

It was initially anticipated that the dextrose saline would be quickly contaminated and permanently colonized and that this would act as a control. It was also expected that the normal saline which is relatively biologically inert would be contaminated as frequently as the contrast media but would not support bacterial growth. Both these expectations proved to be false and we have no explanation for the failure to identify organisms in dextrose saline and normal saline. Dilution and manipulation of the test liquids was performed in as "normal" a non-sterile manner as possible but in order to reduce individual variability these manipulations were performed by only one author (D.L.).

The results show that all contrast media are easily contaminated and can support viable organisms more easily than do either dextrose saline or normal saline. Transmission of contaminating organisms by the operator at the time of sampling seems to be more important at room temperature and in cold solutions than is persistent colonization of contrast media. Persistent colonization does not seem to occur at room tempature or at 4°C. *Bacillus species* were the most frequent contaminating organism at all temperatures and may have colonized ioxaglate at 37°C. *Micrococci* were found mainly at 37°C and may have colonized iohexol at this temperature. Tixobar in a 25% suspension supports contaminants less well than do LOWS media at all three temperatures and there was no evidence of colonization of Tixobar.

This suggests that careful handling—using sterile equipment and sterile water for dilution at the time of investigation and storage at room temperature or at 4°C—may be more important in reducing the incidence of contamination of LOWS media for gastro-intestinal studies than the fact that the container had been opened and its contents part used in the past.

Because LOWS contrast media at 37°C may support the growth of environmental micro-organisms, it is important to store opened containers at 4°C to minimize the multiplication of contaminating micro-organisms.

Conclusion

1. Opened bottles of LOWS contrast media stored in the refrigerator or at room temperature may be used for gastro-intestinal studies providing clean equipment is used on each occasion.
2. Dilute Tixobar is preferable, from a microbiological point of view, to LOWS media isosmolar to plasma, providing the gastro-intestinal tract is intact.
3. Particular care should be taken not to keep opened bottles (or damaged bottles or ampoules) of LOWS media in warming ovens, especially if these media are to be used parenterally.

References

Bell, McKinsky & Mills, 1987. Iopamidol in the diagnosis of suspected upper G.I. perforation. *Clinical Radiology, 38*, 165–168.

Cohen, M. D., 1987. Choosing contrast media for the evaluation of the gastro-intestinal tract of neonates and infants. *Radiology, 162*, 447–456.

Cowan, S. T. & Steele, K. J., 1975. *Manual for the Identification of Medical Bacteria, 2nd edn* (Cambridge University Press, Cambridge).

Dawson, P., Backer, A. & Holton, J. M., 1983. The effect of contrast media on the growth of bacteria. *British Journal of Radiology, 56*, 809–815.

Ginai, A. Z., 1985. Experimental evaluation of various available contrast agents for use in the gastro-intestinal tract in case of suspected leakage. Effect on peritoneum. *British Journal of Radiology, 58*, 969–978.

Lennette, E. H., Balows, A., Hausler, W. J. & Shadomy, H. J., 1985. *Manual of Clinical Microbiology, 4th edn* (American Society for Microbiology, Washington, USA).

Ratcliffe, J. F., 1986. The use of low osmolality water soluble (LOWS) contrast media in the paediatric gastro-intestinal tract. A report of 115 cases. *Paediatric Radiology, 16*, 47–52.

1990, *The British Journal of Radiology*, *63*, 535–536

Assessment of a single lumbar spine radiograph in low back pain

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Abstract. The lumbosacral spine radiographs of 200 patients with unexplained low back pain and without neurological signs were reviewed. The purpose of the study was to determine whether significant diagnostic information would be lost by replacing the standard three film series with a single radiograph, either in the lateral or antero-posterior projection. The contribution of the coned lumbosacral junction view was also assessed. The results show that a single lateral radiograph is diagnostically satisfactory and would have the added advantages of reducing patient radiation dose and radiographic workload.

The use of radiological services needs to be rationalized in order to control increasing demand and reduce patient irradiation. The standard lumbar spine series (antero-posterior (AP), lateral and coned lateral of the lumbosacral junction (LSJ)) account for some 3.5% of all radiological investigations (Brekkan, 1983). In addition, the radiation dose from the standard three film series is considerable, imparting a total body dose of 3.86 mSieverts (mSv). This is equivalent to about 66 low kV chest radiographs, which have an individual dose of approximately 0.058 mSv (IRCP, 1982).

The value of lumbar spine radiography is in doubt when used as an initial investigation in low back pain without obvious cause (Currey et al, 1979; Waddell, 1982; Butt, 1989). The aim of this study was to determine whether a single AP or lateral radiograph could replace the standard three film series, and also to assess the contribution of the coned LSJ view.

Methods

The radiographs of 200 patients referred by their general practitioners with low back pain, and in whom there was no suspicion of malignancy or infection, no history of trauma and no neurological signs, were reviewed by a radiologist (J.B. or R.C.). The patients' radiographs were divided into two equal groups of 100. The AP projection was viewed first in Group 1 and the nature and severity of any abnormality was recorded according to the categories shown in Table I. After subsequent review of the lateral radiograph, any change in the observations was recorded (Table II). Finally, the LSJ film was viewed and any further change in the overall assessment was documented (Table III). The same procedure was used in the second group except that the lateral projection was viewed first.

Results

The influence of the second film on the final assessment (Table II) was found to be greatest when the AP was viewed first (Group 1), resulting in a change in 32% of cases, as compared with 3% when the lateral film was viewed first (Group 2). In 23% of cases in Group 1, a further diagnostic category was added, whilst in 8%, there was an increase in the severity of the pathology demonstrated. In no case was significant diagnostic information lost by examination of a single film, be it

Table I. Diagnostic categories and grades of severity

Category		Severity
1. Normal		
2. Spondylosis	(a)	Minimal osteophytes, no disc space loss
	(b)	Larger osteophytes affecting more than three vertebrae
	(c)	As (b) but with disc space loss
3. Osteoporosis	(a)	No collapse
	(b)	End plate collapse
	(c)	Vertebral body collapse
4. Osteoarthrosis of facet joints and pars defects	(a)	Spondylolysis
	(b)	Spondylolisthesis
	(c)	(a) and (b)
5. Other	*e.g.*	Old osteochondritis

Table II. Influence of additional radiograph on original assessment of a single projection

Change in observations	Group 1 (AP first) (%)	Group 2 (lateral first) (%)
No change	68	97
Change of severity		
Increase	8	0
Decrease	0	0
Addition of further category	23	0
Addition of further category and change in severity		
Increase	0	3
Decrease	1	0

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Table III. Change of report after addition of third radiograph (LSJ) to series

Change in overall assessment	% of total
No change	96
Change	4

the AP or lateral. Additional information was gained from the LSJ view in 4% of cases (Table III). In all of these cases, the junction was excluded from the lateral film or was so underpenetrated as to be uninterpretable. In no case would this additional information have altered patient management.

Discussion

Low back pain is the second largest medical cause of lost work in the UK after chronic bronchitis (British Medical Journal, 1979) and causes more days of lost work than industrial action (Waddell, 1982). As most patients with low back pain recover within a few weeks on conservative management (Currey et al, 1979; Butt, 1989), it can be argued that plain radiography has little to offer in the initial assessment of this condition. Currey et al (1979) have suggested that radiographs should be reserved for second line investigation of those patients whose symptoms have not settled after 3 months of conservative treatment. In addition, they felt that plain radiography had little to offer when the history and examination failed to indicate a specific pathology. Indeed, in those cases where a particular pathology was found, it had generally been suspected prior to the radiographic examination, often to the extent of being documented in the case notes. Neither their findings nor ours support the notion that plain radiographs are justified to detect occasional but unsuspected pathology such as ankylosing spondylitis or metastases. We would concur with their suggestion that the erythrocyte sedimentation rate (ESR) and other simple blood tests are more appropriate initial investigations. With this background, it is not suprising that we have found that limiting the radiological investigations to a single lateral film has no influence on the final diagnosis.

Despite this, it is likely that plain radiographs of the lumbar spine will continue to be requested as the initial investigation of low back pain, a practice which we believe should be increasingly questioned. Although limiting the examination to a single lateral film would appear to be a logical step, it might reasonably be argued that if the value of the test is in doubt it should not be performed at all.

Our study indicates that a single lateral view, obtained using the technique described by Eisenberg et al (1979), would miss no significant pathology demonstrated on the conventional three film lumbar spine series. We suggest that the introduction of a single lateral film policy in patients with low back pain with no apparent or suspected cause should be acceptable medical practice. We do not feel that this could be reasonably opposed on medico-legal grounds. Such a policy would have added the advantages of reducing patient radiation dosage and radiographic workload.

Prior screening of requests for lumbar spine radiographs would determine whether additional films were warranted in any particular clinical situation.

References

BREKKAN, A., 1983. Radiographic examination of the lumbosacral spine: an "age stratified" study. *Clinical Radiology*, *34*, 321–324.

BRITISH MEDICAL JOURNAL, 1979. Back pain—what can we offer? (Editorial). *British Medical Journal*, *2*, 709.

BUTT, W. P., 1989. Radiology of back pain. *Clinical Radiology*, *40*, 6–10.

CURREY, H. L. F., GREENWOOD, R. M., LLOYD, G. G. & MURRAL, R. S., 1979. A prospective study in low back pain. *Rheumatology and Rehabilitation*, *18*, 94–104.

EISENBERG, R. L., ATKIN, J. R. & HEDGCOCK, M. W., 1979. Single well centred lateral view of the lumbosacral spine: is a coned view necessary? *American Journal of Roentgenology*, *133*, 711–713.

ICRP, 1982. Protection of the patient in diagnostic radiology. *Annals of the ICRP*, *9*, 52.

WADDELL, G., 1982. An approach to backache. *British Journal of Hospital Medicine*, *28*, 182–218.

1990, *The British Journal of Radiology*, *63*, 537–541

Skeletal abnormalities in Refsum's disease (heredopathia atactica polyneuritiformis)

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Abstract. Refsum's disease is a rare inborn error of phytanic acid metabolism in which skeletal abnormalities are part of the clinical syndrome. The reported incidence of bone changes in patients with Refsum's disease varies widely and reflects the small series published to date. An analysis of the skeletal abnormalities of the largest series of patients in the world is presented.

Refsum's disease (heredopathia atactica polyneuritiformis) is a rare recessive genetically determined condition caused by the patient's inability to metabolize phytanic acid. As a consequence, the concentration of this fatty acid in the lipid sites of the body and in the plasma rise to high levels. Phytanic acid which is derived from phytol in chlorophyll is found in the highest concentrations in foodstuffs obtained from chlorophyll eating animals (*e.g.* mutton and milk products). The long term treatment is by a low phytanic diet and in severe cases plasma exchange is used.

The clinical syndrome includes three groups of abnormalities (Gibberd et al, 1985):

1. A skeletal dysplasia which is not directly related to phytanic acid levels.
2. Symptoms and signs which develop slowly and do not improve significantly when blood phytanic acid levels fall. This group includes retinitis pigmentosa, anosmia and deafness.
3. Abnormalities directly related to phytanic acid levels and which respond well to a lowering of blood phytanic acid. These include a peripheral neuropathy, ataxia, cardiac arrhythmias and ichthyosis.

Refsum's original description of four cases (1945) recorded the presence of bony abnormalities including shortening and deformity of tubular bones in the hands and feet and an epiphyseal dysplasia of the knees, elbows and shoulders.

By 1965, 28 cases had been published in the world literature and these were reviewed by Richterich et al (1965). The incidence of bone abnormalities calculated from these case reports and small series was reported to be 75%. Since then there have been a sporadic number of single case reports (Rake & Saunders, 1966; Flament-Durand et al, 1971; Fryer et al, 1971) or of single families with several cases amongst the offspring (Campbell & Williams, 1967; Nevin et al, 1967; Wall & Worthington, 1979). In these reports there is a very high incidence of changes in the metatarsals, especially the third and fourth, and the metacarpals as well as less frequent reports of phalangeal changes. These abnormalities are almost invariably bilateral and symmetrical. This paper sets out to describe the skeletal deformities and quantify their incidence in patients with Refsum's disease. This series of patients is the largest number in the world attending a single hospital.

Patients and methods

Complete clinical records and radiological studies were available for 17 patients with biochemically proven Refsum's disease. All patients had radiographs of their hands, feet, elbows, knees and shoulders. Radiographs of the rest of the skeleton were available for many of these patients. Of the 17 patients, 10 were male and seven female; four of the males are brothers and two others are siblings (D. G. and her brother, R. G.) of whom only the sister, D. G., shows bone changes.

Six of the 17 cases studied had skeletal abnormalities.

Brief case histories of these six patients are given with the ages at which the skeletal studies were done. The patients had many estimations of plasma phytanic acid and the level given is representative of the levels prior to treatment, unless otherwise stated. The upper limit of normal of plasma phytanic acid is 33 micromols/l.

Case 1

D. H., a 46-year-old man. His vision had deteriorated at 7 years old, subsequently he developed a peripheral neuropathy at 14 years of age. His plasma phytanic acid was 1605 micromols/l.

Case 2

D. G., a 63-year-old woman. Poor vision was first noticed at 10 years old. At 27 years of age, increasing deafness was ascribed to streptomycin prescribed for tuberculosis one year earlier. Fourteen years later she

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Table I. Skeletal abnormalities present in six out of 17 patients studied

Patient	Sex	Hands		Feet	Elbows	Knees
		1st term. phalanx	Metacarpals	Metatarsals		
1. D.H.	M	+ +	—	+ + (3, 4 & 5)	—	—
2. D.G.	F	+ + (Right side only)	—	—	+	+
3. E.E.	F	+ +	—	+ + (1 & 4)	+	+
4. B.H.	M	+ +	—	+ + (4)	+	+
5. S.S.	F	+ +	—	—	+	+
6. I.F.	F	+ + (& Left 5th mid-phalanx)	+	+ + (4)	—	+

+ + marked
+ definite but not gross

was completely deaf. At 47 years old she developed severe weakness in both legs. Phytanic acid level was 2054 micromols/l.

Case 3

E. E., a 27-year-old woman. She had never been aware of a sense of smell. At the age of 19 years her vision began to deteriorate and 2 years later she noticed numbness of her hands and a generalized dry, scaly skin. Phytanic acid level was 1733 micromols/l.

Case 4

B. H., a 28-year-old man. He became aware of night blindness at 18 years of age and at this time noticed that he had a very dry skin. Two years later his vision had deteriorated markedly. He became increasingly unsteady on his feet and his hearing became progressively impaired. His plasma phytanic acid level was 1059 micromols/l but he had started a low phytanic acid diet just prior to his attendance at Westminster Hospital.

Case 5

S. S., a 28-year-old woman. Reduced visual acuity led to the diagnosis of retinitis pigmentosa at the age of 9 years. She remained well until she was 25 years old when she lost 2 stone in weight and subsequently became unsteady and developed numbness in her legs. She became increasingly deaf and weakness progressed and involved her arms so that she was unable to feed herself. At presentation her phytanic acid level was 6420 micromols/l and she was treated with plasma exchange as well as diet.

Case 6

I. F., a 38-year-old female. She was always aware of a poor sense of smell and mild night blindness; however, retinitis pigmentosa was not diagnosed until she was 28 years old. One year later she started to become deaf. At the age of 35 years her legs became progressively weak and painful so that she had to resort to a wheel chair. She has been on a low phytanic acid diet for some time before attending Westminster Hospital and her phytanic acid was 642 micromols/l.

Radiological findings

Table I lists the skeletal abnormalities which were identified in these six patients.

Terminal phalanges of the thumb

Abnormalities were present in the six patients; in five patients the changes were bilateral (in Case 2, unilateral). There was shortening of the mid-portion of the shaft of the phalanx with a normal proximal articular surface and distal terminal tuft producing a short, conical bone (Fig. 1).

Middle phalanges

Case 6 only.

The left fifth middle phalanx of the hand showed normal articular surfaces at each end of a markedly shortened shaft.

Metacarpals and metatarsals

Metacarpals: Case 6 only. Metatarsals: Cases 1, 3, 4 and 6.

There was shortening of the shafts of these bones (particularly the fourth metatarsal) and marked tapering of the distal shafts (Fig. 2).

Knees

Cases 2, 3, 4, 5 and 6.

The intercondylar notch of the distal femur had a shallow inverted "V" appearance (Fig. 3).

Elbows

Cases 2, 3 and 4.

Irregularity of the distal humerus was identified with flattening of the lateral part of the trochlea (Fig. 4).

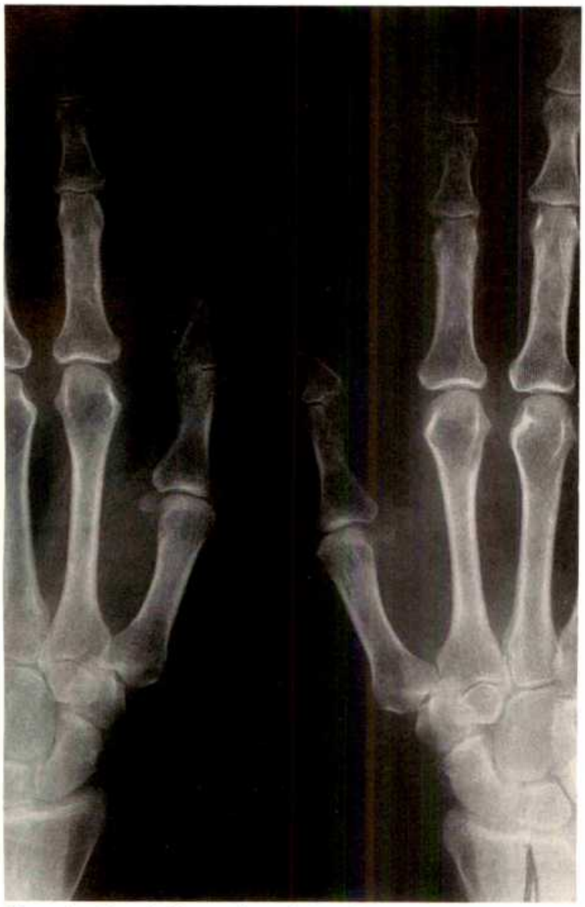

Figure 1. *Case 2.* Shortening of the right terminal phalanx of the thumb giving a conical appearance.

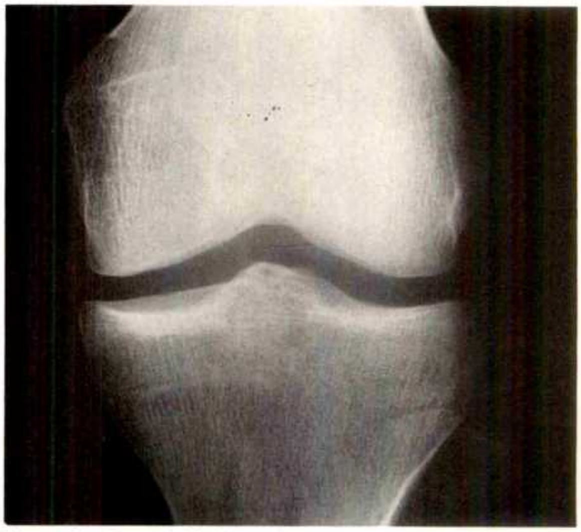

Figure 3. *Case 3.* Shallow "inverted V" appearance of the intercondylar notch of the distal femur.

In addition to these specific abnormalities, many patients had evidence of degenerative changes throughout their skeletons and these changes were considerably more advanced than would be expected for the patient's age.

Although changes were seen in the knees and elbows of most of the patients with skeletal abnormalities, these were sometimes subtle. In Case 6 there were metaphyseal abnormalities throughout the skeleton superimposed on the changes described above. The skeletal changes in this patient were the most severe encountered.

Previous reports, including the original description of Refsum (1945), described changes in the shoulder joint. No such changes were found in our series, neither were

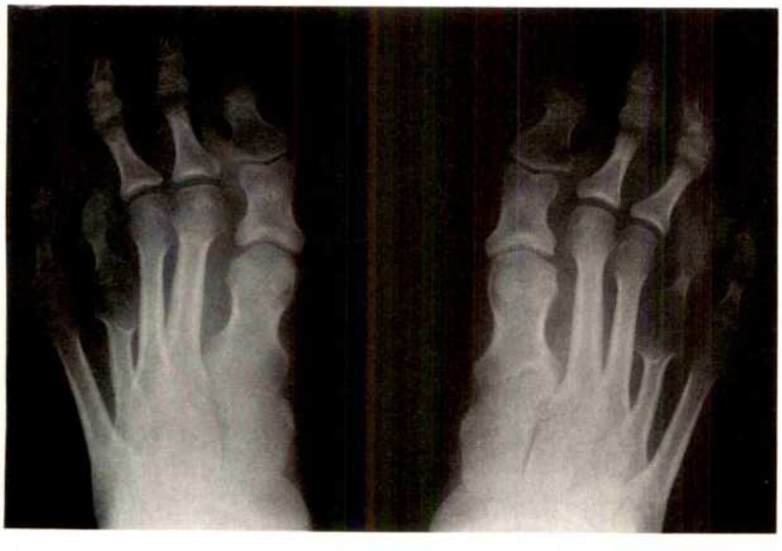

Figure 2. *Case 3.* Marked shortening of the first and fourth metatarsals with a modelling deformity of the first proximal phalanges.

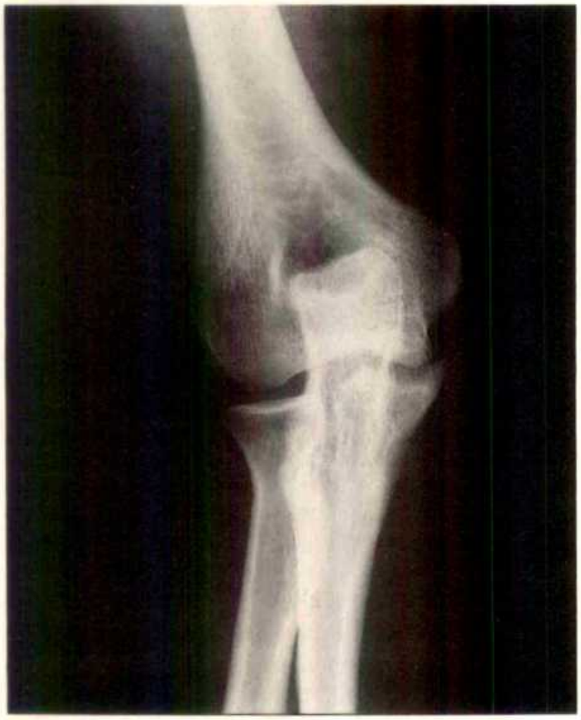

Figure 4. *Case 3.* Flattening of the lateral part of the trochlea of the distal humerus.

the many other types of bony abnormality described by Richterich et al (1965).

Patients with Refsum's disease without bone changes

There were 11 patients with Refsum's disease whose radiographs of the hands, feet, elbows and shoulders were normal. One of these patients (R. G.) was the brother of D. G. who is affected by skeletal changes. The others were unrelated to any of the patients with bone changes. Four of the patients without bone changes are brothers, whilst all others are unrelated to each other.

Relatives of patients with Refsum's disease

Many relatives of patients with Refsum's disease have been examined clinically and some radiologically. Clinically, the parents of one patient (Case 3) appear to have shortened metatarsals but radiographs of their feet are normal. Clinical examination and radiographs on all other relatives were normal.

Discussion

Between the original description by Refsum in 1945 and 1962, a total of 32 patients were described in the world literature (Richterich et al, 1965). By 1975 a total of 58 patients were known (Refsum, 1975). Since then further cases, some with skeletal abnormalities, have been described (Wall & Worthington, 1979).

Previous reports have identified skeletal abnormalities as one of the cardinal features of Refsum's disease but these reports have not always distinguished between the characteristic changes and those attributable to degenerative disease. Richterich et al reviewed the literature in 1965 and suggested an incidence of 50% for the specific changes and 75% if degenerative changes were included. On reviewing their paper, we conclude that only seven (25%) out of the 28 cases reviewed could be described as having bone abnormalities characteristic of Refsum's disease. This corresponds more closely with our experience; in our series of 17 patients the incidence of skeletal abnormalities was six out of 17 (35%). Furthermore, the statement that the skeletal abnormalities in Refsum's disease "are similar to, but milder than, those seen in Thalidomide embryopathy" (Richterich et al, 1965) does not bear close scrutiny.

The most striking abnormalities are the shortened tubular bones in the hands and feet and especially the very short conical terminal phalanx of the thumb which was seen in all patients who had skeletal involvement. It is of interest that of the six thumbs illustrated in the accumulated literature, four show this abnormality (Toussaint et al, 1959; Skre et al, 1969; Wall & Worthington, 1979). The high frequency of this finding has not been previously reported and may prove to be a specific morphological marker of the skeletal changes in Refsum's disease.

Most bone abnormalities are symmetrical on the two sides of the body and in most cases changes are seen in both the hands and feet. There does not appear to be any relationship between the number of the digits affected in the hand compared with that in the foot.

The mechanism and natural history of the skeletal deformities in Refsum's disease are not understood. Richterich et al (1965) proposed that the changes resulted from increased phytanic acid levels, but this seems unlikely in view of the fact that the majority of patients, who all have increased blood phytanic acid levels, do not have any bone changes. Wall and Worthington (1979) suggested a genetic cause, postulating that the disease may be a result of a number of linked genes with varying degrees of expression in each patient.

In the past the skeletal abnormalities of Refsum's disease have been considered to be congenital (Gibberd et al, 1985), but the evidence for this is circumstantial. The patients in this study with clinically obvious differences in metacarpal or metatarsal length, all said that this appearance had been present for as long as they could remember. There is, however, no evidence that these changes were present at birth and it could be that they developed with growth. If these abnormalities are congenital, they must be caused by something other than the inability to metabolize phytanic acid. *In utero*, the blood phytanic acid level is zero. The only possible source of phytanic acid is from the mother's blood and in non-Refsum patients the level of phytanic acid is very low. The disease is a result of an autosomal recessive gene and no mother of a patient with Refsum's disease has ever been shown to have Refsum's disease and therefore no significant amount of phytanic acid can have reached the fetus.

The genetic abnormality in Refsum's disease results in a failure to carry out the alpha-oxidation stage needed for the metabolism of the phytanic acid (Stokke & Eldjarn, 1975). In adults, the only known molecule that requires alpha-oxidation is phytanic acid. It is possible that some other alpha-oxidation process is required in bone development but, if so, it is suprising that not all patients with Refsum's disease develop bone abnormalities. In other respects the clinical features are remarkably constant.

It is possible that the bony changes develop after birth and if this is so, the presence of phytanic acid could be a factor in disturbing the growth of bone. It is thought that the accumulation of phytanic acid takes many years and this is why the disease does not manifest itself early in life. However, some chemical features, such as anosmia and retinitis pigmentosa, characteristically occur earlier in the disease than others, such as ataxia. It could be that the effect of inadequate alpha-oxidation might be manifest at the time of bone development in the early years of life, long before any other manifestations of the disease occur. If this is so, then whether a patient develops bone changes could depend on the diet in infancy. If the diet contained a lot of phytanic acid then bone abnormalities would be more likely. It is known that the later manifestations of the disease, classified as group 3 changes, are very closely related to the dietary level of phytanic acid (Gibberd et al, 1985) and therefore the diet in infancy may be a factor in determining whether or not skeletal abnormalities develop.

In conclusion, about 35% of patients with Refsum's disease develop bone abnormalities which tend to be bilateral and symmetrical. The knees and elbows show epiphyseal flattening and irregular articular margins. The short tubular bones of the hands and feet are most often affected. In particular the terminal phalanx of the thumb is short and conical and this seems to be the single most constant bone abnormality.

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References

Campbell, A. M. G. & Williams, E. R., 1967. Natural History of Refsum's syndrome in a Gloucestershire family. *British Medical Journal, 3,* 777–779.

Flament-Durand, J., Noel, P., Rutsaert, J., Toussaint, D., Malmendier, C. & Lyon, G., 1971. A case of Refsum's disease: clinical, pathological, ultrastructural and biochemical study. *Pathologia Europaea, 6,* 172–191.

Fryer, D. G., Winckleman, A. C., Ways, P. O. & Swanson, A. G., 1971. Refsum's disease. A clinical and pathological report. *Neurology, 21,* 162–167.

Gibberd, F. B., Billimoria, J. D., Goldman, J. M., Clemens, M. E., Evans, R., Whitelaw, M. N., Retsas, S. & Sherratt, R. M., 1985. Heredopathia atactica polyneuritiformis: Refsum's disease. *Acta Neurologica Scandanavica, 72,* 1–17.

Nevin, N. C., Cumings, J. N. & McKeown, F., 1967. Refsum's syndrome (Heredopathia Atactica Polyneuritiformis). *Brain, 90,* 419–428.

Rake, M. & Saunders, M., 1966. Refsum's disease: a disorder of lipid metabolism. *Journal of Neurology, Neurosurgery and Psychiatry, 29,* 417–422.

Refsum, S., 1945. Heredoataxia hemeralopica polyneuritiformis—et tidligere ikke beskrevet familiaert syndrom? *Nordisk Medicin, 28,* 2682–2685.

—— 1975. Heredopathica Atactica Polyneuritiformis: Phytanic acid storage disease (Refsum's disease). In *System Disorders and Atrophies, Part 1. Handbook of Clinical Neurology, Vol. 21,* ed. by P. J. Vinhen and G. W. Bruyn (North Holland Publishers' Company, Amsterdam), pp. 181–229.

Richterich, R., Moser, H. & Rossi, E., 1965. Refsum's disease (Heredopathia atactica polyneuritiformis). An inborn error of lipid metabolism with storage of 3, 7, 11, 15, tetramethyl Hexadecanoic acid. A review of the clinical findings. *Humangenetik, 1,* 322–332.

Skre, H., Eldjarn, L., Stokke, O. & Try, K., 1969. A new case of Heredopathia atactica polyneuritiformis (Refsum's disease). In *Proceedings of the 2nd International Congress of Neurogenetics and Neuro-ophthalmology of the World Federation of Neurology, Montreal,* ed. by A. Barbeau and J.-R. Brunette (Excerpta Medica, Amsterdam), pp. 710–721.

Stokke, O. & Eldjarn, L., 1975. Biochemical and dietary aspects of Refsum's disease. In *Peripheral Neuropathy,* ed. by Dyck et al (W. B. Saunders, Philadelphia, USA), pp. 872–881.

Toussaint, D., Coers, C. & Toppet, N., 1959. Heredopathia atactica polyneuritiformis (Syndrome de Refsum). Constatations cliniques et Biopsiques. *Bulletin de la Société Belge d'Ophthalmologie, 122,* 383–402.

Wall, W. J. H. & Worthington, B. S., 1979. Skeletal changes in Refsum's disease. *Clinical Radiology, 30,* 657–659.

1990, *The British Journal of Radiology*, *63*, 542–546

The effect of ultrasound on the cytoxicity of adriamycin

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Abstract. The effect of continuous wave ultrasound exposures on the cytoxicity of adriamycin has been studied. It has been found that 2.6 MHz, 2.3 Wcm^{-2} (spatial average) ultrasound can enhance the cell killing potential of adriamycin both in suspensions of single V79 chinese hamster fibroblast cells and in spheroids formed from these cells. The ratio of the slopes of the survival curves for single cell suspensions is 1.5. For spheroids, the growth delay is increased by 1.3 days by simultaneous ultrasound exposure. Flow cytometric studies of the intracellular concentration of adriamycin following ultrasound exposure reveals that this is increased when compared with that measured when the cells are only exposed to adriamycin. Evidence is presented to suggest that this is a non-thermal effect of ultrasound.

Ultrasound is one of the methods of choice for the induction of hyperthermia for cancer therapy. Hyperthermia is used not only as a single modality, on its own, but also in conjunction with radiotherapy or chemotherapy. For this reason, it seems sensible to study the effect of ultrasound exposures on the cytotoxic action of chemotherapy agents, both at physiological and at hyperthermic temperatures.

There are a few reports in the literature concerning the effect of ultrasound on drug toxicity. Kremkau et al (1976) studied the survival on mice inoculated with L1210 Leukaemia cells that had been exposed to nitrogen mustard or to nitrogen mustard and ultrasound. They found that animals receiving cells that had been exposed to both nitrogen mustard and ultrasound had a significantly higher survival rate after 3 weeks than those that had received cells that had been exposed either to the drug alone or to ultrasound alone. The authors stated that the "increased cytotoxicity cannot be explained solely on the basis of a conventional thermal mechanism of action", although the maximum temperature rise measured in cell suspensions following ultrasound exposure was 5–6°C.

Senepati et al (1982) looked at the effect of ultrasonically induced hyperthermia on the toxicity of cyclophosphamide, melphalan and procarbazine in human tumour xenografts (MX-1 and LX-1) in mice *in vivo*. They allowed the tumour temperature to rise to 43°C, and found evidence for a synergistic effect of ultrasound hyperthermia and melphalan on MX-1 tumours, and between ultrasound hyperthermia and procarbazine on LX-1 tumours.

Akimoto (1985) studied the effect of the *in vivo* exposure of murine tumours to ultrasound and Mitomycin C. They found that the combined treatment significantly enhanced the amount of inhibition of tumour growth and increased the animals' survival rate. It was speculated that this was caused by an effect of ultrasound on membrane permeability. The tumour temperatures in this study were constrained to be below 35°C, as they were in the work reported by Yumita et al (1987). Yumita et al studied the effects of ultrasound on daunomycin and adriamycin (ADM) toxicity in rats bearing Yoshida sarcoma. They found synergistic effects when ultrasound was combined with either drug. Interestingly, ultrasound exposure alone caused an inhibition in tumour growth, even though the tumour temperature was held below 35°C.

We have embarked on a systematic investigation of the effect of ultrasound on a number of antitumour drugs *in vitro*. This report concerns the effect of ultrasound on ADM toxicity to cells in suspensions and to spheroid cultures.

Adriamycin is an anthracycline antibiotic. It is known to intercalate with DNA. The cell surface is also thought to be a target for ADM action. (Karczmar & Tritton, 1979; Born & Eichholtz-Wirth, 1981). It is known that ADM cytotoxicity is enhanced by hyperthermia (Bleehen, 1984).

Materials and methods

Cell and spheroid culture

Chinese hamster lung fibroblasts V79–379A were grown in suspension using methods described elsewhere (Stratford & Adams, 1977). The cells were maintained in log phase at concentrations ranging between 10^5 and 10^6 per ml. These cells have a doubling time of 10–12 h, and therefore need diluting daily.

When spheroids were required, 5×10^4 cells were inoculated into 10 ml of Eagles Minimum Essential Medium (MEM) plus 10% fetal calf serum (fcs) contained in 90 mm Petri dishes base-coated with 1% agar (noble, Difco). The dishes were kept in an air/5% CO_2 incubator at 37°C for 2 days until small clumps of cells were seen. The medium was then replaced and the culture split into two or three Petri dishes. After 4–5 days the spheroids had reached approximately 200 μm in diameter and were put into spinner flasks with fresh medium. The medium was replaced daily (West, 1983).

Cell and spheroid assays

(i) *Cells.* After treatment, cells were washed by centrifugation and resuspension, counted, serially diluted, plated in MEM + 15% fcs, and incubated at 37°C in an atmosphere of 95% air plus 5% CO$_2$ for 7 days. Colonies containing more than 30 cells were scored as survivors and the surviving fraction was calculated as the number of colonies scored divided by the initial number of cells plated.

The surviving fraction, or plating efficiency, of control cells maintained at 37°C was routinely greater than 0.84. Survival curves were plotted for which the logarithm of surviving fraction was expressed as a function of dose (either drug concentration, or exposure time).

(ii) *Spheroids.* Following treatment, spheroids were washed by centrifugation and resuspension, and spheroids of the required size were selected and put into individual microwells (Linbro 17 × 15 mm) which had been coated with 1% Agar Noble. In any one experiment, 12 spheroids were selected for each experimental point. Two diameters at right angles were measured using a calibrated graticule on an inverted microscope, immediately after treatment, and daily thereafter. Spheroid volumes were calculated using the formula

$$\text{volume} = \frac{4}{3}\pi\,(\text{radius})^3$$

where the radius is taken as the average of the two measured radii.

Growth curves were constructed, for which

$$\log\left[\frac{\text{volume}}{\text{initial volume}}\right]$$

was plotted as a function of time after treatment. Growth delay was taken as the difference in time taken to reach six times the initial volume for the different treatment conditions as compared to the control.

Ultrasound exposures

All ultrasound exposures were carried out using the experimental system described in detail elsewhere (ter Haar et al, 1980, 1988). A 2.6 MHz plane transducer (2.5 cm diameter) was mounted at the bottom of a thermostatically controlled water bath, at an angle of 45° to the horizontal, tilted upwards. An 8 ml aliquot of the sample suspension was inoculated into a cylindrical stainless steel chamber with acoustically transparent windows, (25 mm in diameter). The chamber was then mounted parallel to the transducer face, at a distance of 25 cm, the position of the last axial maximum. The ultrasonic beam hitting the water surface after transmission through the chamber is reflected through 90° away from the primary beam, thus avoiding standing waves. Chambers containing control cell suspensions were also placed in the tank, but away from the ultrasonic beam. Spatially averaged intensities were measured using a tethered float radiometer (Shotton, 1980).

All intensities quoted here are spatial averages. The acoustic pressure profile across the beam was measured using a PVDF membrane hydrophone calibrated at the National Physical Laboratory (GEC Marconi). Sample pressure profiles taken 26 cm from the transducer are shown in Fig. 1. The profiles with and without the chamber in place are shown. It can be seen that the profiles are not changed appreciably by the presence of the sample holder.

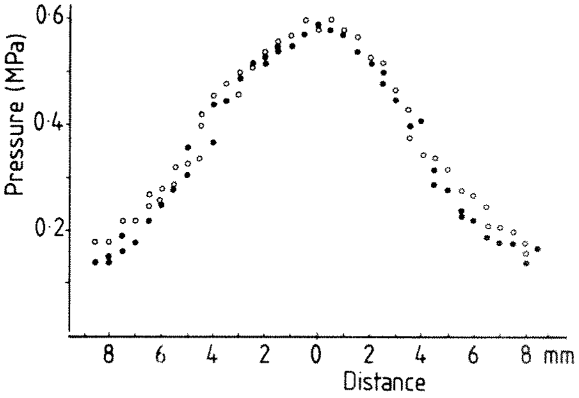

Figure 1. Transverse beam plot at the position of the sample holder. The pressure profile was obtained using a PVDF membrane hydrophone. The profiles are shown both with the sample holder in position (○) and with it removed (●).

Adriamycin exposure

Adriamycin was obtained from Montedison Pharmaceuticals Ltd. The contents of a 10 mg vial were dissolved in 5 ml of sterile water and kept frozen as stock solution. For each experiment, 0.5 ml of stock solution was diluted with PBS to give a 1000 μM solution of ADM (molecular weight 543.8) which was kept in the dark. An appropriate volume was added to the cell suspension immediately before loading into the exposure chamber. Suspensions were exposed at a concentration of 2.10^5 cells/ml for 1 h. Immediately after exposure the suspensions were removed from the chamber, spun down, washed and resuspended in phosphate buffered saline and then assayed in the manner described above.

Temperature studies

In an attempt to determine the effect of small changes in temperature on ADM toxicity, some cell suspension experiments were carried out in the stainless steel chambers with the water bath held at temperatures in the range 37–40°C.

Flow cytometry studies

An Ortho Cytofluorograf 50 H equipped with a lexel 50 mW argon-ion laser tuned to 488 nm and an Ortho 2150 computer system was used. The parameters measured were forward and orthogonally scattered light and ADM flourescence (> 520 nm). The cells were gated on scattered light and fluorescence was displayed on a univariate histogram. The mean channel number from the histogram was recorded and used as a measure of intracellular ADM concentration.

Results

(i) *Single cells in suspension.* Figure 2 shows the survival curve for cells exposed to ADM concentrations in the range 1–8 μM for 1 h at 37°C. The data shown is averaged over eight experiments and the error bars show the standard error of the mean. A linear regression analysis has been performed on the data.

Figure 2 also shows the survival curve for cells exposed simultaneously to ultrasound (2.6 MHz, 2.3 Wcm^{-2} spatial average, continuous wave) and ADM (1–6 μM) for 1 h at 37°C. It can be seen that the ultrasound has rendered the ADM more toxic. The ratio of the slopes of the survival curves with and without ultrasound is 1.5. Ultrasound alone at this intensity at 37°C does not affect cell survival (Fig. 3).

(ii) *Spheroids.* Figure 4 shows the growth curves for 200 μm diameter spheroids exposed to 8 μM ADM, with and without simultaneous ultrasound treatment, and for control spheroids maintained at 37°C without drug or ultrasound treatment. These are averaged over five experiments. Twelve spheroids were measured for each treatment condition, for each experiment.

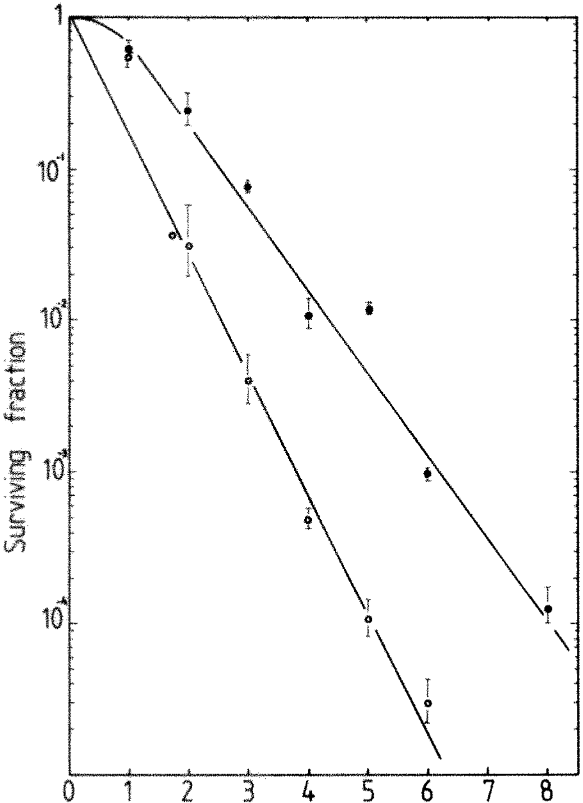

Figure 2. Survival curves showing surviving fraction as a function of adriamycin concentration at 37°C, 60 min exposures, (●) and showing surviving fraction as a function of adriamycin concentration at 37°C for cells exposed simultaneously to adriamycin and continuous wave ultrasound (2.6 MHz; 2.3 Wcm^{-2} spatial average) for 60 min (○).

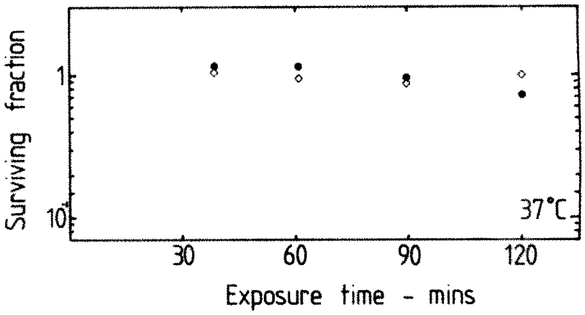

Figure 3. Survival curve showing surviving fraction as a function of time for control cells (●) and for cells exposed to ultrasound alone at 37°C. (2.6 MHz; 2.2 Wcm^{-2} spatial average) (◇).

When averaged over five experiments (60 spheroids), it was found that the time to reach six times their volume at treatment for 200 μm diameter spheroids exposed to 8 μM ADM was 1.9 (±0.2) days longer than for the control group, whereas it took 3.2 (±0.3) days

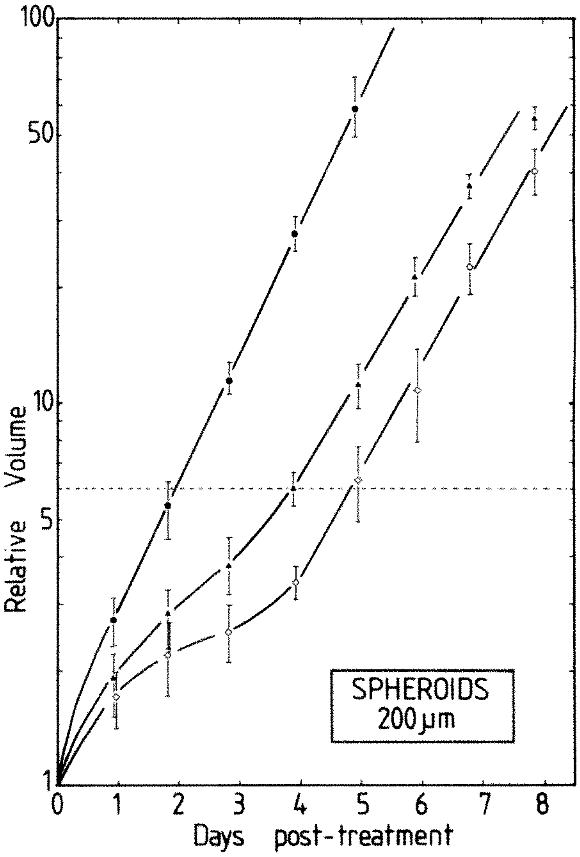

Figure 4. Growth curves for V79 spheroids (200 μm diameter). Curves are shown for control spheroids (●), for spheroids exposed to 8 μM adriamycin (▲) and for spheroids exposed simultaneously to 8 μM adriamycin and continuous wave ultrasound (◇).

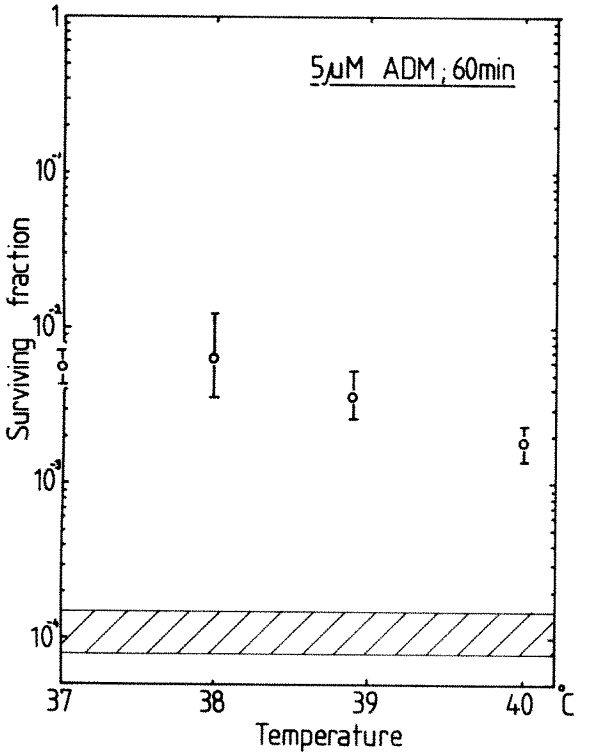

Figure 5. Survival curve showing surviving fractions for cells exposed to 5 µM adriamycin for 60 min at different temperatures. The hatched area shows the survival of cells exposed to adriamycin and ultrasound for 60 min at 37°C.

longer for spheroids subjected to the combination of ultrasound and ADM.

Similar effects were seen with 400 µm diameter spheroids. Averaged over three experiments, the growth delays were found to be 1.2 (±0.4) days for the ADM alone treatment, and 2.1 (±0.5) days for the combined ADM and ultrasound exposure.

(iii) *Temperature studies.* Figure 5 shows the surviving fractions for cells exposed to 5 µM ADM for 1 h while being maintained at elevated temperatures (38°C, 39°C and 40°C). The survival does not change significantly from that of the control (37°C) until a temperature of 40°C is reached. Also marked on Fig. 5 is the surviving fraction for 5 µM ADM + ultrasound at 37°C.

(iv) *Flow cytometry studies.* When separate samples of cells were treated identically with adriamycin, the mean channel numbers of the ADM fluorescence lay within ±3.5%. If cells were treated in suspension with ADM and then held at 37°C, their fluorescence gradually decreased owing to efflux of adriamycin from the cells. This effect was inhibited, but not completely eliminated, by Verapamil. Verapamil is a calcium influx blocker, and has been shown to inhibit drug efflux (Helson, 1984). Thereafter, cells were held on ice immediately after treatment with ADM.

When single cell suspensions were incubated with 5 µm ADM, the ratio of the mean channel number of ADM fluorescence for cells treated with ADM plus ultrasound to that for ADM alone was 1.16±0.05 (average of measurements made on five separate occasions). For cells in spheroids treated with 8 µM ADM, the ratio was 1.24±0.07. If the cells were incubated at 37°C after treatment, these ratios were maintained despite the loss of adriamycin from the cells.

Discussion

The investigations described here have been designed to address the question as to whether ultrasound exposures can modify the toxicity of adriamycin to cells. We have shown that the effect of adriamycin is greater if cells are exposed simultaneously to the drug and to ultrasound. The ultrasound intensity used is not sufficient to cause any change in cell survival on its own at 37°C. The effect is seen both in single cell suspensions and in spheroids.

It is well known that the toxicity of ADM is enhanced at hyperthermic temperatures (Hahn et al, 1975). Previous studies have shown that the ultrasonically induced temperature rise in these cell suspensions under these exposure conditions is no more than 0.2°C (ter Haar et al, 1980). This has been re-confirmed for the work discussed here (data not shown). The temperature studies performed here have demonstrated that the level of cell killing obtained from the combination of 5 µM ADM and ultrasound is considerably greater than that obtained from 5 µM ADM when the cells are maintained at 40°C, a temperature elevation of 3°C above normal. Thus, it seems unlikely that the ultrasound effects seen are a result of bulk heating effects. Although the intraspheroid temperatures have not been measured, it can be shown theoretically that spheroids of the sizes used here cannot maintain a temperature significantly above that of their suspending medium.

The mechanism by which the ADM cytoxicity is enhanced is still unknown. The flow cytometry results indicate that there is an increase in intracellular ADM concentration following ultrasound exposure. However, the increases seen (~16%–25%) do not account in full for the increase in toxicity. At 5 µM, the level of cell killing achieved by the combined exposure is the same as that achieved by 8 µM ADM in its own. This is an effective increase of 60%. There may be a number of reasons that the full apparent increase in ADM concentration is not measured by flow cytometry, a major one being that the efflux of ADM from cells is extremely rapid following washing, and there is a time delay between the end of treatment and measurement on the flow cytometer. The addition of Verapamil inhibits this efflux but does not prevent it.

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References

AKIMOTO, R., 1985. An experimental study on enhancement of the effect of anti-cancer drug by ultrasound. *Journal of the Japanese Society of Cancer Therapy, 20,* 562–570.

BLEEHEN, N. M., 1984. Hyperthermia with drugs: current status. *Strahlentherapie, 160,* 721–724.

BORN, R. & EICHHOLTZ-WIRTH, H., 1981. Effect of different physiological conditions on the action of adriamycin on chinese hamster cells *in vitro. British Journal of Cancer, 44,* 241–246.

TER HAAR, G. R., STRATFORD, I. J. & HILL, C. R., 1980. Ultrasonic irradiation of mammalian cells *in vitro* at hyperthermia temperatures. *British Journal of Radiology, 53,* 784–789.

TER HAAR, G. R., WALLING, J., LOVEROCK, P. & TOWNSEND, S., 1988. The effect of combined heat and ultrasound on multicellular tumour spheroids, *International Journal of Radiation Biology, 53,* 813–827.

HAHN, G. M., BRAUN, J. & HAR-KEDAR, I., 1975. Thermochemotherapy: synergism between hyperthermia (42–43) and adriamycin (or bleomycin) in mammalian cell inactivation. *Proceedings of the National Academy of Sciences of USA, 72,* 937–940.

HELSON, L., 1984. Calcium channel blocker enhancement of anticancer drug cytotoxicity—a review. *Cancer Drug Delivery, 1,* 353–361.

KARCZMAR, G. S. & TRITTON, T. E., 1979. The interaction of adriamycin with small unilamellar vesicle liposomes. A fluorescence study. *Biochimica et Biophysica Acta, 557,* 306–319.

KREMKAU, F. W., KAUFMANN, J. S., WALKER, M., BURCH, P. & SPURR, C. L., 1976. Ultrasonic enhancement of nitrogen mustard cytotoxicity in mouse leukaemia. *Cancer, 37,* 1463–1647.

SENEPATI, N., HOUCHENS, D., OVEJERA, A., BEARD, R. & NINES, R., 1982. Ultrasonic hyperthermia and drugs as therapy for human tumour xenografts. *Cancer Treatment Reports, 66,* 1635–1639.

SHOTTON, K. C., 1980. A tethered float radiometer for measuring the output power from ultrasonic therapy equipment. *Ultrasound in Medicine and Biology, 6,* 131–133.

STRATFORD, I. J. & ADAMS, G. E., 1977. Effect of hyperthermia on the differential cytotoxicity of a hypoxic cell radiosensitizer Ro-07-0582, on mammalian cells *in vitro. British Journal of Cancer, 35,* 307–313.

WEST, C. M. L., 1983. The effect of cytotoxic drugs and radiation on mammalian cells and multicellular spheroids *in vitro. PhD Thesis* (University of London).

YUMITA, N., OKUMURA, A., NISHIGAKI, R., VNEMURA, K. & UMEMURA, S., 1987. The combination treatment of ultrasound and antitumour drugs on Yoshida Sarcoma. *Japanese Journal of Hyperthermic Oncology, 3,* 175–182.

1990, *The British Journal of Radiology*, *63*, 547–553

Comparison of 5-Fluorouracil pharmacokinetics following intraperitoneal and intravenous administration using *in vivo* ^{19}F magnetic resonance spectroscopy

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Abstract. Intrahepatic pharmacokinetic studies of 5-Fluorouracil (5 FU) metabolism following intravenous and intraperitoneal administration have been undertaken in four patients using *in vivo* ^{19}F nuclear magnetic resonance spectroscopy. Following intravenous administration, 5 FU decayed with "half times" ranging from 5 to 17 min. There was considerable variation of 5 FU pharmacokinetics between patients following intraperitoneal administration. Peritoneal contamination by infused 5 FU was considered to be a significant problem in one patient. A technique for providing superficial signal suppression was therefore investigated and its efficacy for excluding signal from the peritoneal space has been demonstrated. Owing to the potential for contamination from peritoneal 5 FU, the accumulation of fluoro-beta-alanine (FBAL) is a more reliable indicator of drug catabolism than the measurement of unlocalized "hepatic" 5 FU. Rapid intrahepatic catabolism of 5 FU to FBAL was demonstrated in all patients. However, there was greater pharmacokinetic variation following intraperitoneal administration than following intravenous administration. Therapeutic implications of intravenous compared with intraperitoneal administration of 5 FU are discussed.

Hepatic metastasis from the gastrointestinal tract is facilitated by the extensive portal venous system. Adenocarcinomas of the colon and rectum are amongst the most frequent of malignant tumours in the West (Souhami & Tobias, 1986) with liver metastases present in 20% of patients at presentation and in over 80% of patients with recurrent disease (Taylor et al, 1985). Locoregional recurrence at the site of bowel anastomisis or elsewhere within the peritoneal cavity occurs in up to 75% of patients at the time of initial failure (Prosnitz et al, 1983). Once macroscopic metastatic disease has become established treatment is at best palliative.

5-Fluorouracil (5 FU) is the cytotoxic agent most commonly used for the palliation of advanced gastrointestinal malignancy. The drug is well tolerated with minimum toxicity, however the reported response rate is only of the order of 20–25% (Carter et al, 1976). Generally the drug is administered by intravenous or oral routes and the maximum dose that can be administered is mainly limited by hepatic and haematological toxicity (Sugarbaker et al, 1985). 5-Fluorouracil is primarily catabolized by the liver, whereas the anabolic pathway predominates in peripheral normal tissues and in tumours. Anabolism proceeds along two main pathways through biotransformation into fluoronucleosides thence to form fluoronucleotides following phosphorylation (Fig. 1). The cytotoxicity of 5 FU is mainly considered to result from formation of fluoro-deoxyuridine-monophosphate (FdUMP) which inhibits thymidylate synthetase, and from incorporation of the drug into ribo-nucleic acid (RNA) (Curt et al, 1984). Cellular sensitivity to 5 FU has been shown to be related to different rates of intracellular drug metabolism rather than to variation of cellular uptake of the parent drug (Laskin et al, 1979).

Intraperitoneal administration of 5 FU is a novel treatment approach and may offer the advantages of increased concentration of drug in the peritoneal cavity, high portal blood concentration and reduced systemic toxicity (Dedrick et al, 1985). Following intraperitoneal administration of 5 FU in human subjects, the drug concentration has been shown to be four times greater in portal venous blood compared with that sampled from a peripheral artery or vein or from the hepatic vein. Furthermore, up to 70% of the drug is extracted by the liver at first pass (Speyer, 1985). The therapeutic index will depend upon the relative concentrations of drug in normal liver and extrahepatic tissues compared with intrahepatic tumour. Comparison of intraperitoneal *versus* intravenous administration of 5 FU as adjuvant chemotherapy in patients with colorectal carcinoma demonstrated reduced haematological and hepatic toxicity allowing administration of higher drug doses through the former route; however, the incidence of subsequent liver metastases was not reduced and there was no improvement in survival (Sugarbaker et al, 1985). By contrast, 5 FU administered directly into the

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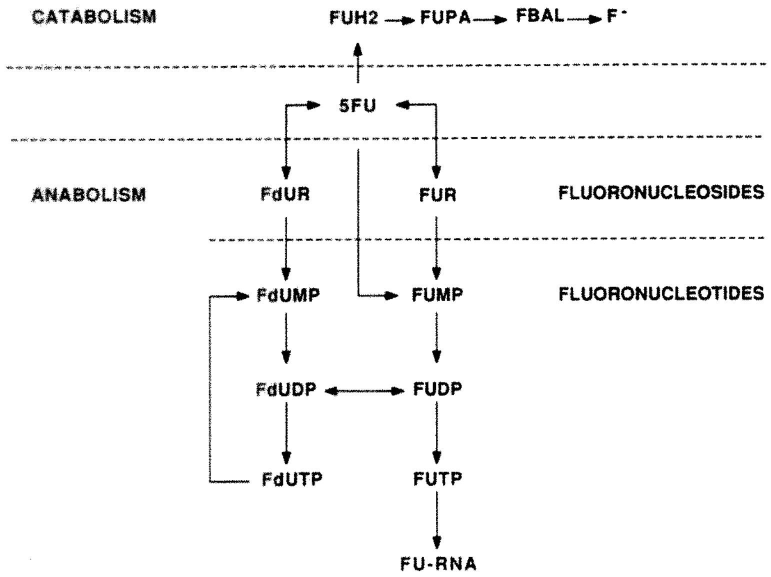


Figure 1. 5-Fluorouracil: metabolic pathways.

portal vein has been shown to reduce the incidence of liver metastases and improve survival in a similar group of patients (Taylor et al, 1985). Although macroscopic metastases may derive their blood supply predominantly from the hepatic arterial system rather than the portal system (Sigurdson et al, 1987), the blood supply of microscopic metastases might be less specific.

In vivo ^{19}F magnetic resonance spectroscopy (MRS) provides a non-invasive technique for measurement of 5 FU metabolism in the liver (Stevens et al, 1984; Wolf et al, 1987a). The degree and rates of metabolism of 5 FU can be measured in normal liver and in tumour and offers the possibility of elucidating mechanisms of drug resistance. This report describes the results of a preliminary study comparing hepatic 5 FU metabolism following intravenous with intraperitoneal administration in four patients using *in vivo* whole body ^{19}F MRS.

Materials and methods

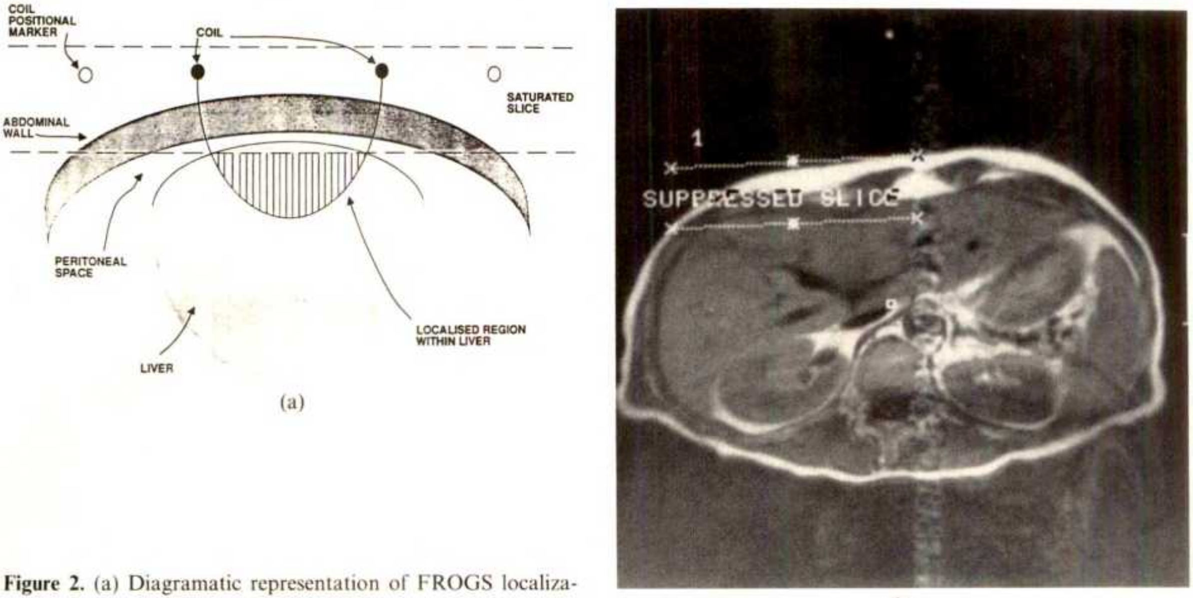
Four patients undergoing treatment with 5 FU chemotherapy for recurrent gastrointestinal adenocarcinoma have been studied. Pre-treatment evaluation included liver ultrasound or computerized tomography for documentation of hepatic involvement. One patient had confirmed liver metastases whilst there was no evidence of liver involvement in the other three patients. If ascites was present it was drained prior to intraperitoneal administration of 5 FU.

For intraperitoneal administration an intraperitoneal catheter was inserted through the midline of the lower abdominal wall under local anaesthesia. Intravenous 5 FU was given through a canula inserted into a peripheral arm vein. For each route of administration a total dose of 1 g of 5 FU was delivered over 10 min. The drug was prepared in 250 ml of normal saline for intraperitoneal administration and in 150 ml normal saline for intravenous administration.

Examinations were performed using a 1.5 Tesla Siemens Magnetom whole body nuclear magnetic resonance system. A transmit/receive coil with a 17 cm diameter was positioned on the anterior abdominal wall overlying the liver. All lines necessary for drug administration were attached prior to positioning the patient in the magnet. Proton localizing images were acquired immediately after positioning the patient in the magnet in order to relate the position of the coil, which included a localizing marker containing doped water, to the underlying liver. 5 FU was administered by the selected route following completion of magnetic field shimming.

In the first patient examined (B.A.), following intraperitoneal 5 FU, it was thought that signal originating from 5 FU in the peritoneal space overlying the liver was unlikely. However, observation of the 5 FU results in patient M.U. indicated that there was a significant problem and subsequent abdominal radiographic examination revealed that the intraperitoneal catheter was positioned adjacent to the liver. Therefore, for subsequent patients, S.M. and L.U., this phenomenon was further explored by applying the "fast rotating gradient selection" (FROGS) sequence (Sharp et al, 1987) adapted for use with fluorine in order to provide superficial signal suppression, the method being interleaved between some of the unlocalized free induction decay (FID) pulse and acquire sequences.

The FROGS (localized) sequence was used to saturate the magnetization within a superficial slice positioned parallel to the coil in order to eliminate signal from this region. The detected signal originates primarily from a region defined by the coil response beyond the slice (Fig. 2a). The sequence consists of a series of selective sinc pulses of differing amplitude which tip the sample magnetization into the XY plane where it is dephased by spoiler gradients. Application of the read pulse follows a delay period to allow decay of



(a)

(b)

Figure 2. (a) Diagramatic representation of FROGS localization technique. (b) Proton localization image.

induced eddy currents. Before data acquisition the z magnetization within the slice has been largely eliminated by the saturation pulses and therefore contributes little signal. The sequence employed a repetition time of 2 s and a dwell time of 100 μs. The slice thickness and orientation necessary to eliminate signal from the peritoneal space was defined individually for each patient using a proton image of the region of interest (Fig. 2b).

The FID (unlocalized) sequence used a repetition time of 2 s and a dwell time of 130 μs. Sets of 2 or 4 min acquisitions were collected. Sequential measurements were undertaken from the time of commencing drug administration and were continued for up to 80 min thereafter.

Data was processed by exponential multiplication in the time domain centred at time 0, followed by fast Fourier transformation. Constant and frequency-dependent phase corrections were applied. Peak integration was undertaken using the "real part" of the data.

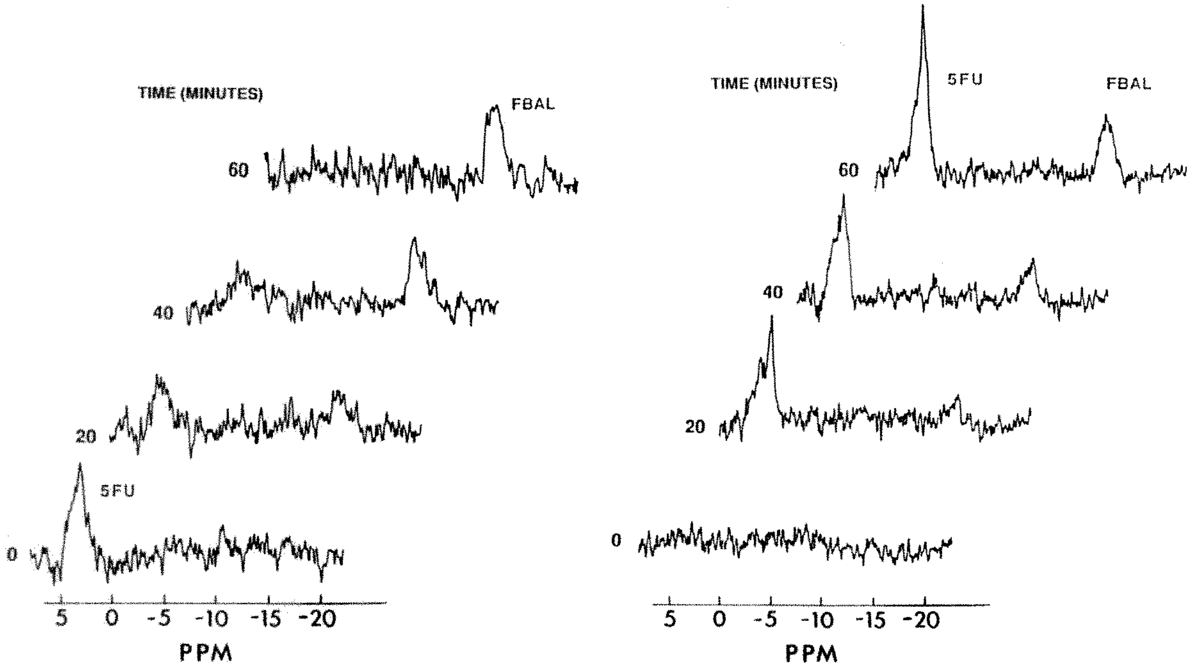
Results

The time course of hepatic 5 FU metabolism following intravenous and intraperitoneal administration using the surface coil without FROGS localization from patient B.A. are shown as sequential spectra in Fig. 3. Following intravenous administration the 5 FU signal can be seen after 4 min, decreasing until no longer visible at 56 min. In contrast, following intraperitoneal administration the signal due to 5 FU rises steadily from 13 min until the end of the examination as a result of transperitoneal absorption. The broad peak at -14 ppm is mainly composed of fluoro-beta-alanine (FBAL) but may also include unresolved fluoro-ureido-propionic acid (FUPA). Henceforth this will be referred to only as FBAL. Following intravenous and intraperitoneal administration the pharmacokinetics of FBAL are similar, appearing at approximately 20 min and continuing to increase until the end of each examination.

Unlocalized spectroscopy over the liver demonstrated changes in the observed 5 FU concentration with time following intravenous administration in all four patients (Fig. 4a). When 5 FU was administered by this route the signal decayed with "half times" ranging from 5 to 17 min.

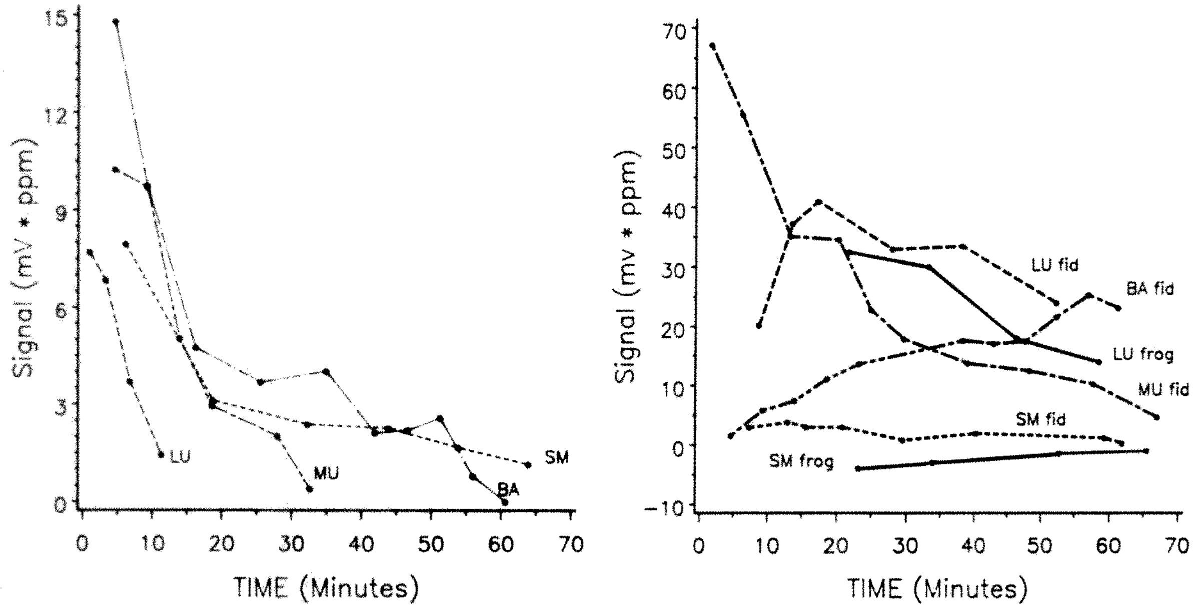
Following intraperitoneal administration the unlocalized spectra demonstrated considerable inter-patient variation in the uptake and decay of 5 FU. In patients L.U. and S.M., in addition to unlocalized FID measurements, data were also acquired using the superficial suppression technique commencing approximately 20 min after drug administration. In patient L.U., the rate of decay of 5 FU was similar for both unlocalized and localized measurements, although the latter produced a lower overall signal. In patient S.M. a small but significant 5 FU signal was detected in the unlocalized spectra but not when using the superficial suppression technique (Fig. 4b). Comparison of localized and unlocalized summed spectra measured from the same starting point in this patient are shown in Figs 5a and 5b, respectively.

FBAL, the principal catabolite of 5 FU, was detectable in the livers of all patients following both intravenous and intraperitoneal administration. With FBAL, the problem of peritoneal contamination does not arise because it is an intrahepatic catabolite. Following both intraperitoneal and intravenous administration, hepatic levels of FBAL accumulated rapidly in the patients examined, reaching equilibrium between 41 and 63 min after 5 FU administration (Fig. 6). No other catabolites



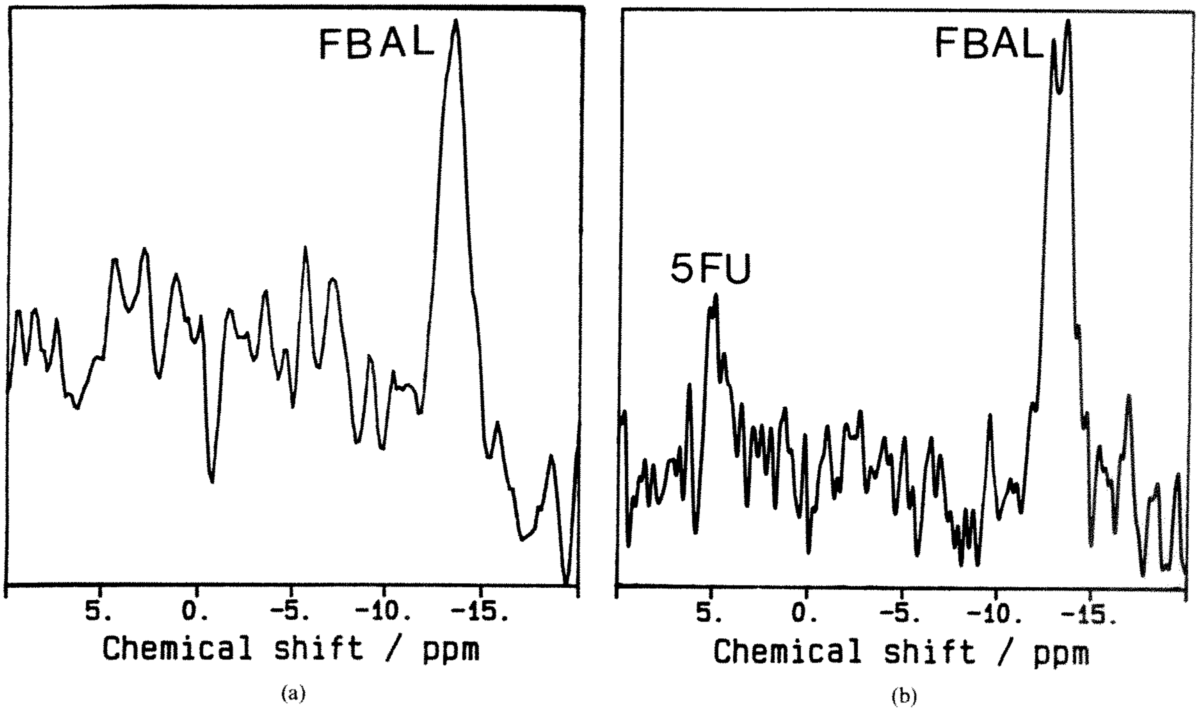
(a) (b)

Figure 3. (a) 5 FU kinetics: intravenous 5 FU: sequential ^{19}F spectra commencing immediately after drug administration (time = 0) in patient B.A. (b) 5 FU kinetics: intraperitoneal 5 FU: sequential ^{19}F spectra commencing immediately after drug administration (time = 0) in patient B.A.



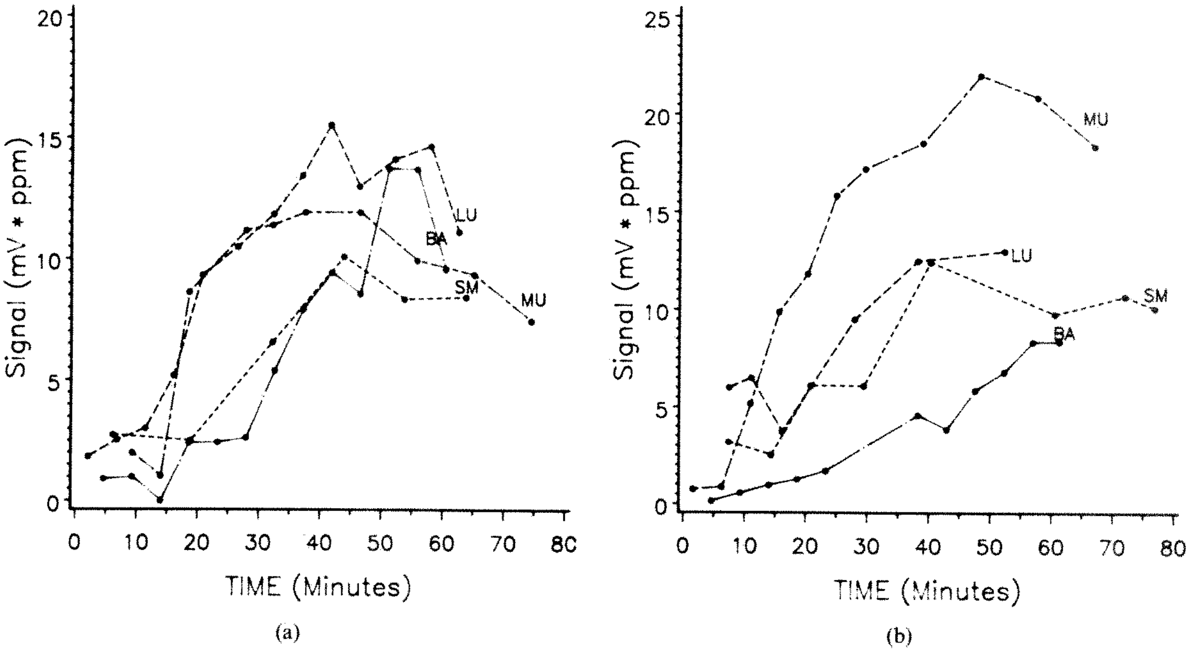
(a) (b)

Figure 4. (a) 5 FU kinetics: 5 FU time course following intravenous administration. (b) 5 FU kinetics: 5 FU time course following intraperitoneal administration. Key: fid, unlocalized data (broken lines); frogs, localized data (solid lines).



(a) (b)

Figure 5. (a) Patient S.M.: summated spectrum demonstrating FROGS suppression of signal from intraperitoneal 5 FU. (b) Patient S.M.: summated unlocalized FID spectrum demonstrating signal contamination from intraperitoneal 5 FU.



(a) (b)

Figure 6. (a) FBAL kinetics: FBAL time course following intravenous administration of 5 FU. (b) FBAL kinetics: FBAL time course following intraperitoneal administration of 5 FU.

were detected at significant levels. Using existing processing methods, fluoronucleotides and fluoronucleosides, anabolites of 5 FU metabolism, were not apparent at significant concentrations in any of the measurements including those of patient S.M. who was known to have intrahepatic tumour within the region of examination.

Discussion

In vivo ^{19}F MRS has been used successfully to investigate 5 FU metabolism in normal murine liver and in murine tumours (Stevens et al, 1984). The technique has also been used to compare intravenous with intraperitoneal drug administration in Sprague–Dawley rat mammary tumours in which FBAL and FUPA were both detected, but only following intravenous administration (Koutcher et al, 1987). *In vivo* human ^{19}F MRS has only recently become possible following the advent of whole body spectrometers (Wolf et al, 1987a). Using a 1.5 Tesla NMR whole body system we have been able to detect 5 FU and FBAL in human liver *in vivo* and to compare hepatic pharmacokinetics following intravenous and intraperitoneal administration.

Following intravenous administration of 5 FU a rapid rise in intrahepatic concentration was observed in all patients with subsequent decay of the parent drug. "Half times" ranged from 5 to 17 min (Fig. 4a).

Following intraperitoneal administration, we observed considerable pharmacokinetic variation of 5 FU using unlocalized measurements (Fig. 4b). The rate of increase of intrahepatic 5 FU in patient M.U. after intraperitoneal infusion was similar to that following intravenous administration with a maximum concentration of 5 FU immediately after drug administration, decaying rapidly thereafter. The apparent rapid liver uptake in this case is most probably an artefact resulting from the inadvertent intraperitoneal infusion of 5 FU over the peritoneal surface of the liver.

Spectral localization using the FROGS technique demonstrated a lower level of 5 FU in patient L.U. compared with unlocalized measurements. However when measured over comparable time periods, the localization method completely eliminated the 5 FU signal in patient S.M. (Fig. 4b). The absence of signal in this case may be the result of rapid intrahepatic drug catabolism.

As the FROGS technique is known to provide good suppression of signal within the selected region, the differences between the localized and unlocalized spectra are most probably the result of suppressing peritoneal contamination by 5 FU. The degree of contamination will depend principally upon catheter position but may also be influenced by disturbance of peritoneal anatomy following surgery and by the rate of drug absorption. A further factor that will affect the relative sensitivity of the two measurements is the suppression of superficial hepatic signal, where a part of the liver is included within the suppressed plane.

Reasons for the wide variation in 5 FU liver uptake and decay following intraperitoneal administration, therefore, include contamination from the peritoneal space and also variation of the position of the intra-abdominal catheter, peritoneal abnormalities caused by disease or previous surgery, post-prandial portal blood flow variation and differences in the rates of drug metabolism.

Care must be taken in the interpretation of 5 FU kinetics from unlocalized measurements recorded over the liver. The results from patients L.U. and S.M. demonstrate that a method of localization is advisable. Future studies will employ a localization technique in all patients and larger volumes of intraperitoneal infusate.

Intrahepatic catabolism of 5 FU to FBAL was observed in all patients (Figs 6a and 6b). Following both intravenous and intraperitoneal administration of 5 FU the rates of accumulation of FBAL were similar, reaching equilibrium between 41 and 63 min. This may be the result of saturation of the catabolic pathway (Hull et al, 1988). The accumulation of FBAL reflects the rate of hepatic 5 FU catabolism more accurately than the disappearance of 5 FU in this study because there is no intraperitoneal contamination of the spectrum by FBAL. We are at present, with existing processing methods, unable to detect short lived anabolites, fluoronucleosides or fluoronucleotides in the patient with liver metastases, possibly owing to the poor signal to noise ratio. Anabolism of 5 FU has been demonstrated *in vivo* in a human squamous cell carcinoma but was not detected in the normal liver (Wolf et al, 1987b). However fluoronucleotides have been demonstrated by *in vitro* high resolution ^{19}F MRS in normal human liver biopsies following systemic administration of 5 FU (Hull et al, 1987). ^{19}F MRS has also demonstrated fluoronucleotides and fluoronucleosides in isolated mouse liver perfused with 5 FU both by direct examination and in perchloric acid extracts (Cabanac et al, 1988).

In summary, our results demonstrate the value of *in vivo* MRS for non-invasive observation of chemotherapy metabolites and pharmacokinetics in patients. The rapid appearance of FBAL has confirmed rapid absorption of 5 FU from the peritoneal space. Although higher liver concentrations of 5 FU might be achieved following intraperitoneal administration, further work will be required to confirm this. Magnetic resonance spectroscopy offers the prospect of *in vivo* investigation of primary and acquired resistance to 5 FU (Wolf et al, 1988) and the investigation of pharmacological modification of drug metabolism in tumours. From the preliminary results obtained using the FROGS suppression sequence it is clear that there is a possibility of 5 FU from the intraperitoneal space contaminating unlocalized measurements. Therefore, if unlocalized measurements are used, conclusions should only be drawn from the accumulation of metabolic products such as FBAL.

In order to ensure tumour specificity, accurate spatial localization is essential. In future, a Conformal ISIS technique will be employed to localize signal from within tumour and to optimize the signal to noise ratio (Sharp & Leach, 1989). Quantitation using an external fluorine source is currently being developed and further clinical studies of liver and tumour metabolism are being pursued.

Acknowledgments

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References

CABANAC, S., MALET-MARTINO, M. C., BON, M., MARTINO, R., NEDELEC, J. F. & DIMICOLI, J. L., 1988. Direct ^{19}F NMR spectroscopic observation of 5-Fluorouracil metabolism in the isolated perfused mouse liver. *NMR In Biomedicine, 1,* 113–120.

CARTER, S. K., 1976. Large bowel cancer. The current status of treatment. *Journal of the National Cancer Institute, 56,* 3–10.

CURT, G. A., ALLEGRA, R. L., FINE, G. C., YEH, G. C., JOLIVET, J. & CHABNER, B. A., 1984. Fluoropyrimidines in cancer chemotherapy. In *The E.O.R.T.C. Cancer Chemotherapy Annual,* Ed. by H. M. Pinedo and B. A. Chabner (Elsevier, Oxford), pp. 8–14.

DEDRICK, R. L., 1985. Theoretical and experimental bases of I.P. chemotherapy. *Seminars In Oncology, XII, Suppl. 4 (Sept),* 1–6.

HULL, W. E., PORT, R., KUNZ, W. & SCHLAG, P., 1987. ^{19}F-N.M.R. for monitoring 5-Fluorouracil chemotherapy. *Journal of Cancer Research and Clinical Oncology, 113,* S46.

HULL, W. E., PORT, R. E., HERRMAN, R., BRITSCH, B. & KUNZ, W., 1988. Metabolites of 5-Fluorouracil in plasma and urine, as monitored by ^{19}F nuclear magnetic resonance spectroscopy, for patients receiving chemotherapy with or without methotrexate pretreatment. *Cancer Research, 48,* 1680–1688.

KOUTCHER, J. A., BARNETT, D. C., MARTIN, D. S., STOFFI, R., SAWYER, R. & COWBURN, D., 1987. In vivo ^{19}F N.M.R. studies of agents altering 5 FU metabolism. *Proceedings of The Society of Magnetic Resonance in Medicine, 6th Annual Meeting* (SMRM, California, USA), 108.

LASKIN, J. P., EVANS, R. M., SLOCUM, H. K., BURKE, D. & HAKALA, M. T., 1979. Basis for natural variation in sensitivity to 5 FU in mouse and human cells in culture. *Cancer Research, 39,* 383–390.

PROSNITZ, L. R., KAPP, D. S. & WEISENBERG, J. B., 1983. Medical Progress: Radiotherapy. *New England Journal of Medicine, 309,* 771–777.

SHARP, J. C. & LEACH, M. O., 1989. Conformal NMR spectroscopy: accurate localisation to non-cuboidal volumes with optimal signal to noise ratio. *Magnetic Resonance in Medicine, 11,* 376–388.

SHARP, J. C., LEACH, M. O., HIND, A., MCCREADY, V. R., WEBER, H. & SAUTER, R., 1987. F.R.O.G.S.: a surface coil 31-P spectroscopy localisation technique. *Proceedings of The Society of Magnetic Resonance in Medicine, 6th Annual Meeting, New York* (SMRM, California, USA), 600.

SIGURDSON, E. R., RIDGE, J. A., KEMENY, N. & DALY, J. M., 1987. Tumour and liver drug uptake following hepatic artery and portal vein infusion. *Journal of Clinical Oncology, 5,* 1836–1840.

SOUHAMI, R. & TOBIAS, J., 1986. In *Cancer And Its Management* (Blackwell Scientific, Oxford), p. 278.

SPEYER, J. L., 1985. The rationale behind intraperitoneal chemotherapy in gastrointestinal malignancies. *Seminars in Oncology, XII, Suppl. 4 (Sept),* 23–28.

STEVENS, A. N., MORRIS, P. G., ILES, R. A., SHELDON, P. W. & GRIFFITHS, J. R., 1984. 5-Fluorouracil metabolism monitored by ^{19}F N.M.R. *British Journal of Cancer, 50,* 113–117.

SUGARBAKER, P. H., GIANOLA, F. J., SPEYER, J. L., WESLEY, R., BAROFSKY, I. & MYERS, C. E., 1985. Prospective randomised trial of I.V. versus I.P. 5 FU, in patients with advanced primary colon or rectal cancer. *Seminars in Oncology, XII, Suppl. 4 (Sept),* 23–28.

TAYLOR, I., MACHIN, D., MULLEE, M., TROTTER, G., COOKE, T. & WEST, C., 1985. A randomised controlled trial of adjuvant portal vein cytotoxic perfusion in colorectal cancer. *British Journal of Surgery, 72,* 359–363.

WOLF, W., ALBRIGHT, M. J., SILVER, M., WEBER, H., REICHARDT, U. & SAUER, R., 1987a. Fluorine 19 N.M.R. spectroscopic studies of the metabolism of 5 Fluorouracil in the liver of patients undergoing chemotherapy. *Magnetic Resonance Imaging, 5,* 165–169.

WOLF, W., ALBRIGHT, M., SAUTER, R., REICHARDT, U., SILVER, M., WEBER, H. & SAUER, R., 1987b. Non-invasive studies of drug metabolism: NMR spectroscopy of 5-Fluorouracil in patients with squamous cell carcinoma of the head and neck. *Proceedings of the Annual Meeting of the American Association of Cancer Research, 28,* 189.

WOLF, W., PRESANT, C. A., ALBRIGHT, M. J., SERVIS, K. L., BARKER, P., RING R., EL-TAHTAWY, A., ATKINSON, D. & KING, M. E., 1988. F-19 M.R. spectroscopy of 5-FU as a method of noninvasive monitoring of drug targeting and delivery. *Radiology, 169,* 84.

1990, *The British Journal of Radiology*, 63, 554–556

Smoking and mucosal reactions to radiotherapy

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Abstract. The pattern of cigarette smoking of 41 patients receiving continuous, hyperfractionated, accelerated radiotherapy for locally advanced head and neck cancer was examined to determine any relationship with the duration of mucositis. The uniformity of the treatment given made it possible to perform an analysis of the factors influencing the duration of the mucositis. There was no correlation with age, sex or weight loss prior to treatment. A highly significant correlation was shown with smoking during and/or after treatment ($p = 0.014$) and with the volume of mucosa irradiated ($p = 0.025$). Both appeared to act independently. It is important to encourage patients to cease smoking totally, prior to radiotherapy, to minimize the duration of mucositis associated with radiotherapy.

In the radiotherapy of head and neck cancer, the regimen chosen is influenced by the expected early and late radiation reactions in the normal tissues included; of these the mucous membrane is of particular importance. The dose per fraction, overall time and total dose given, together with the amount of mucosa included in the treatment volume, all determine the severity of the early reaction and the time required for it to settle. It has been noted that alterations in dose of only 5–10% may cause marked changes in the intensity and duration of the mucosal reaction (Fletcher, 1980). Radiotherapists recognize the presence of sepsis, recent trauma (including surgery), alcohol, smoking and possibly nutritional status as other aggravating factors, but these have been difficult to quantify. Coincidental or associated disease in the mouth such as the changes associated with "beetle nut" chewing may also influence the response. There appears to be a considerable individual variability which may be independent of all the factors described.

Using an accelerated scheme of radiotherapy, such as continuous, hyperfractionated, accelerated radiotherapy (CHART), it is the early reactions that are dose limiting and, in the follow-up of patients treated at Mount Vernon, there was an impression that delay in healing may have been related to cigarette smoking. An investigation of the factors influencing the duration of early mucosal reactions was undertaken.

Materials and methods

From January 1985 to May 1989, 112 patients with advanced head and neck tumours were treated at Mount Vernon Hospital with the CHART regimen (Saunders et al, 1988, 1989). The radiotherapy employed incorporated 36 fractions over a continuous period of 12 days with a 6 h gap between the first and second and between the second and third treatments on each day. Treatment began on a Monday morning and was completed on the second Friday evening, treating daily. A 5 MeV linear accelerator was employed for all treatment. Initially a minimum tumour dose of 1.4 Gy was given in each of 36 fractions to give a total dose of 50.4 Gy. A "large volume" was given a minimum tumour dose of 42 Gy in 30 fractions over 10 days and the final 6 fractions were given to a "reduced volume" so as to achieve the total of 50.4 Gy. After initial experience on 11 patients, the dose per fraction was increased to 1.5 Gy, the large volume receiving 42 Gy in 28 fractions and the small volume 12 Gy in 8 fractions to give a total of 54.0 Gy in 36 fractions.

Out of the 112 patients treated for head and neck tumours, 44 patients were treated for tumours at sites that did not involve irradiation of oral or oro-pharyngeal mucosa (*e.g.* larynx, columella, parotid). For 24 of the remaining 68 patients, data were not available (18 were dead and six had been treated too recently for analysis). Data were therefore available concerning 44 patients. However, three further patients were excluded as the volume of the oral and oropharyngeal mucosa irradiated was less than 20% and reactions could not be compared to those occurring in the other cases.

The 41 patients included 14 women and 27 men and the mean age was 61 years (range: 18–83 years). The mean weight loss prior to treatment was 1.78 kg (range: 3.6 kg gain–12.5 kg loss). Four of the 41 patients received a total dose of 50.4 Gy, the remaining 37 were given 54.0 Gy. Data were routinely collected prospectively in all these patients before, during and after treatment and entered on proformas for subsequent transfer to the departmental computer for data analysis. After it was observed that patients who were known to be smoking appeared to have prolonged mucosal reactions, further data concerning smoking were gathered retrospectively for patients who had received radiotherapy to the oral cavity and oropharynx, and added to the data base. Great care was taken to encourage patients to be truthful in their answers. Although alcohol consumption during and after radiotherapy was also of interest, experience led to the view that reliable data would not be obtainable from these patients.

The smoking patterns of the patients were examined

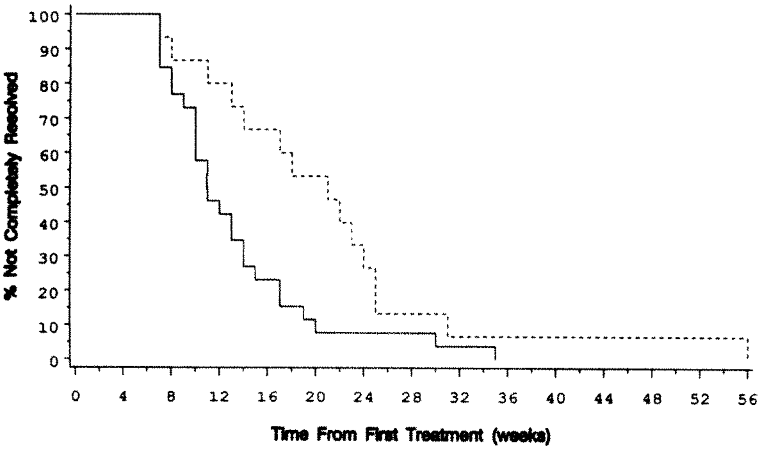

Figure 1. Life table plot showing the time from Day 1 of treatment to full recovery of the mucosa for all patients not smoking at the time of treatment and Groups 3 and 4 patients who smoked during and/or after treatment. The difference is significant at the $p=0.014$ level by the log rank test. —— Groups 1 + 2 ($n=26$); - - - Groups 3 + 4 ($n=15$).

and it was found that they could be placed in one of four groups.

(1) Patients who either had never smoked, or had given up at least 3 years before the appearance of their tumour.

(2) Patients who smoked up to the time of radiotherapy, but who had stopped at its commencement and never re-started.

(3) Patients who abstained during the radiotherapy and for a 4 week period following the treatment, but then resumed smoking.

(4) Patients who continued to smoke throughout treatment and during subsequent follow-up.

All patients receiving CHART showed a full membranous reaction in areas included in both large and small volumes. This appeared on Days 13–15 in the large majority and persisted 8–24 weeks after the first day of treatment before final complete disappearance. The area within the small volume, and particularly the tongue, was the last to settle. Usually the patient returned to a normal diet in 8–10 weeks and the areas of delayed healing gave rise to minimal symptoms. The duration of the mucositis was recorded as the time from Day 1 of treatment to the date on which the mucositis was first noted to be completely resolved.

As a further assessment of the influence of the amount of mucosa irradiated the proportion of the oral and oropharyngeal mucosa irradiated was calculated by reviewing the treatment fields, simulator portal films and treatment plans. This was performed for each patient for both the small and the large volume. Three groups of patients were defined. Group A included patients who had the whole, or practically the whole, of their oral and oropharyngeal mucosa included in both the large and small volume, Group C included patients who had less than 50% of their oral and oropharyngeal mucosa treated in the large volume but more than 20% in the small volume and Group B included the remaining patients who fell between Groups A and C.

Results

There was no correlation between the duration of mucositis and age ($p=0.023$), sex ($p=0.48$) or weight loss ($p=0.074$) using Spearman correlation analysis. There was a significant correlation with smoking pattern ($p=0.014$) and also with the amount of mucosa irradiated in the small volume ($p=0.025$), but not with the large volume ($p=0.34$). Smoking pattern and the area of the small volume were independent variables influencing the duration of mucositis. The relationship of these two

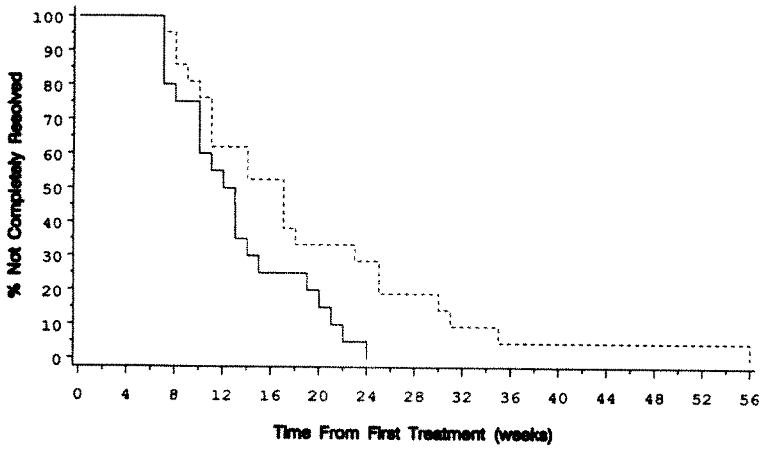

Figure 2. Life table plot showing the time from Day 1 of treatment to full recovery of the mucosa for all patients divided according to the volume of mucosa irradiated. An arbitrary cut off of 50% of the small volume was taken. The difference is significant at the $p=0.025$ level by the log rank test. —— $\leqslant 50\%$ ($n=20$); - - - $>50\%$ ($n=21$).

Table I. Mucositis duration according to smoking group

Patient group	Number of patients	Day 1 to resolution of mucositis (weeks)
1 Never smoked	8	12.4
2 Stopped before radiotherapy	18	13.6
3 Temporary abstinence	7	18.3
4 Continued to smoke throughout treatment	8	23.4

Patient smoking patterns and the mean duration of mucositis for each group from Day 1 of treatment to the date mucositis first noted to be completely resolved.

Table II. Duration of mucositis and mucosal volume irradiated

Proportion of oral and pharyngeal mucosa irradiated	Group according to smoking pattern (number of patients)	Weeks from Day 1 of radiotherapy to complete resolution of mucositis (mean duration in weeks)	
Group A (all or nearly all)	1 (0)	—	20
	2 (6)	18	
	3 (3)	23	
	4 (0)	—	
Group B (intermediate)	1 (6)	12	17
	2 (6)	13	
	3 (2)	15	
	4 (4)	30	
Group C (less than half)	1 (2)	12	13
	2 (6)	10	
	3 (2)	14	
	4 (4)	16	
Total	41		

Division of patients according to the proportion of the oral and oropharyngeal mucosa irradiated and the pattern of cigarette smoking with the mean duration of mucositis from Day 1 of treatment to the date mucositis was first noted to be completely resolved, for each group.

variables to the overall duration of mucositis is shown in life tables (Figs 1 and 2). The mean duration of the mucositis in patients grouped according to patterns of cigarette smoking is shown in Table I. If the patients who either never smoked at all (Group 1) or stopped before treatment (Group 2) are combined, the duration of mucositis was 13 weeks compared with 21 weeks in patients who did smoke at any time after the onset of treatment (Groups 3 and 4).

In Table II the patients have been divided into three groups according to the amount of oral and pharyngeal mucosa irradiated and, as in Fig. 2, there appears to be a direct relationship between the amount irradiated and the duration of mucositis. Within each of the Groups A, B and C there is a trend for the duration of mucositis to be related to smoking pattern.

Discussion

CHART is unusual in that the entire course is finished before the patient starts to develop any reaction at all, and so the regimen is strictly adhered to in every case. This has given us a sensitive situation in order to determine the factors influencing the duration of mucositis. This study has demonstrated the importance of smoking upon the duration of mucositis in our patients. It has also demonstrated that the amount of mucosa irradiated to the full minimum tumour dose directly influences the duration of mucositis, as evidenced by significant correlation with the small volume. Age, sex and weight loss (reflecting nutritional status) appear not to influence the duration of mucositis.

In accelerated radiotherapy regimens such as CHART, where early mucosal reactions are dose limiting, the elimination of cigarette smoking can almost halve the duration of mucositis. Under the conditions of conventionally fractionated radiotherapy the effect is likely to be present, but may not be as marked. We have noted that where mucosal reactions heal quickly, complete recovery to normal appearance commonly occurs, whereas a prolonged period of reaction is often associated with a permanently thinned and atrophic appearance. A measure such as the discontinuation of cigarette smoking may therefore reduce late changes.

A number of patients with head and neck cancer cease cigarette smoking when the diagnosis is made and others can be persuaded to do so. Many, however, find it difficult to do so, but for those who are to be treated by radiotherapy the importance is clear and every effort should be made to inform them of the situation and to encourage them to abandon the habit.

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References

FLETCHER, G. H., 1980. *Textbook of Radiotherapy, 3rd Edition* (Lea & Febiger, Philadelphia), p. 291.

SAUNDERS, M. I., DISCHE, S., FOWLER, J. F., DENEKAMP, J., DUNPHY, E. P., GROSCH, E., FERMONT, D., ASHFORD, R., MAHER, J. & DES ROCHERS, C., 1988. Radiotherapy employing three fractions on each of twelve consecutive days. *Acta Oncologica, 27,* 163–167.

SAUNDERS, M. I., DISCHE, S., HONG, A., GROSCH, E., FERMONT, D., ASHFORD, R. U. & MAHER, E. J., 1989. Continuous hyperfractionated accelerated radiotherapy in locally advanced carcinoma of the head and neck region. *International Journal of Radiation Oncology, Biology, Physics, 17,* 1287–1293.

1990, *The British Journal of Radiology*, *63*, 557–561

Glutathione and cysteine levels in human tumour biopsies

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Abstract. There is evidence that some human tumours could be treated with a combination of buthionine sulfoximine and hypoxic cell sensitizers. However, clinical application of this technique requires a prior knowledge of the level of non-protein bound sulfhydryl (NPSH) compounds in these tumours. The present study provides data on the levels of glutathione (GSH) and cysteine (CYS) in human tumour biopsies from the cervix and from the head and neck. The NPSH compounds were measured by high performance liquid chromatography. The median GSH values were 20.5 nmol/mg protein (cervix) and 23 nmol/mg protein (head and neck) while the median CYS values were 4.4 (cervix) and 4.2 nmol/mg protein (head and neck). The values varied widely from one patient to another.

The results of a number of studies have suggested that non-protein bound sulfhydryl (NPSH) compounds, especially glutathione (GSH), play a fundamental role in cellular radiosensitization *in vitro* (Biaglow et al, 1983; Brown, 1983; Revesz & Malaise, 1983). Intracellular cysteine (CYS) may also play a major role in cellular radiosensitivity: it is an effective radioprotector (Bacq, 1965) and also a precursor of GSH (Reed et al, 1983). More often than not, when GSH is depleted, the oxygen enhancement ratio (OER) tends to be reduced as hypoxic cells become more radiosensitive. It may thus be possible to radiosensitize tumours containing a high percentage of hypoxic cells by reducing their GSH content. The specific γ-glutamylcysteine synthetase inhibitor, buthionine sulfoximine (BSO), can radiosensitize hypoxic cells *in vitro*. Its *in vivo* radiosensitizing activity is rather low, but it frequently increases the radiosensitizing activity of misonidazole (MISO) (Yu & Brown, 1984; Guichard et al, 1986; Ono et al, 1986). However, there is not always a link between this extra-radiosensitization and the decrease of the intracellular GSH level (Guichard et al, 1986). There may be two explanations for this lack of relationship. The GSH level may not be lowered enough, *in vivo*, to be effective; it has been shown that it is difficult to reduce the GSH level below 4% of initial value (Minchinton et al, 1984; Rojas et al, 1984; Yu & Brown, 1984; Guichard et al, 1986; Ono et al, 1986). It is also possible that the absolute GSH level is more important than the percentage of reduction of GSH level. Clinical application of a combination of BSO and MISO will require detailed data on the GSH levels in human tumours, especially if the absolute GSH level is shown to be the pivotal factor.

The aim of this study was to measure the GSH and cysteine levels in human tumour biopsies from two groups of cancers: the cervix and the head and neck (mainly carcinomas) using high performance liquid chromatography (HPLC).

Materials and methods

Biopsies were taken from two groups of cancers, cervix (under general anaesthesia) and head and neck (under local anaesthesia). The total number of patients was 42. Within a few seconds after biopsy, samples were frozen in liquid nitrogen and stored at −70°C until thiol extraction was performed. Portions of the same samples were examined histologically, after fixation in Bouin's fluid (cervical biopsies) or AFA (head and neck biopsies). Five micron sections were prepared using standard techniques and stained with hematoxylin-eosin-safran. The percentages of normal tissue, tumour and necrotic tissues in each biopsy were estimated using a modification of the technique previously used by Dische et al (1986) (simple visual impression). From enlarged projections and/or photographs of the sections the outlines of the tumour, normal and necrotic areas were traced onto paper; the areas were cut out and weighed; the percentage of each zone was then calculated.

Thiol analysis

High performance liquid chromatography. Biopsies were cut in small fragments, the fragments were suspended in 2 ml of 0.2 M Tris buffer, 1 mM EDTA, homogenized and sonicated. GSH and CYS were determined using monobromobimane (mBBr). The technique was similar to that used previously with human tumour xenografts (Guichard et al, 1986). Protein content was determined by the Sedmak and Grossberg method (Sedmak & Grossberg, 1977).

In a preliminary set of experiments, human tumour xenografts were also used; they were excised and cut in

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two fragments. One fragment was immediately frozen and kept at −70°C for 4 weeks before it was analysed, the second one was analysed immediately.

Results

The effect of storage at −70°C on GSH and CYS levels was assessed using human tumour xenografts: GSH and CYS levels did not differ in the frozen and unfrozen samples.

Cervix (Table I).

Biopsies were taken from areas outside detectable necrotic zones. The patient was examined under general anaesthesia and the disease stage assessed in terms of the International Federation of Gynecology and Obstetrics (FIGO) classification. The tumour size, expressed as two-dimensional measurements, involved only the visible cervical or cervico-vaginal lesion; it was assessed by clinical examination and by taking an alginate vaginal cast. This size is correlated with the FIGO stage of pelvic regional involvement. There was some disagreement in Patients 1, 2 and 18, between the histological data and the FIGO stage (Table I): all patients suffered from an invasive cervical cancer, the diagnosis was based on biopsies which were quite independent of the series taken for GSH assay and histopathological examination.

Two tumour biopsies were taken from Patients 2 and 4. The GSH levels were similar in the two biopsies from Patient 2, but were slightly different in those from Patient 4.

Glutathione content (nmol/mg protein). For non-irradiated cancer patients: the median GSH content of 18 patients was between 22.8 and 24.4 (extremes: 5.7 and 55.2). No correlation was found between the GSH content and either the tumour size (squamous cell carcinomas), the cancer stage or its degree of differentiation.

Table I. Glutathione and cysteine in cervix biopsies

Patient	Histology	Stage (FIGO)	Size (cm) D: diameter	GSH	CYS	% Tumour in biopsy
				in nmol/mg protein		
Non-irradiated patients						
1	Carcinoma *in situ*	I	D:4	26.8	4.5	10
2	Microinvasive carcinoma	II		5.7	3.0	40
				5.7	1.3	
3	Squamous cell carcinoma	I	D:4	12.4	2.4	58
4		I	D:4	30.6	4.4	100
				39.1	5.1	
5		I	D:5	33.0	0.3	89
6		II	7/8	16.3	2.1	19
7		II	D:5	38.5	4.6	68
8		II	D:4	38.2	4.2	57
9		II	small tumour	24.4	8.0	42
10[a]		III	D:2.5	19.8	0.8	66
11		III	6/4	22.8	5.0	22
12		III	D:7	47.6	2.5	100
13		III	D:4	31.4	0	84
14		III	5/4/4	17.2	7.2	77
15		III	D:6	21.1	4.8	32
16	Adenocarcinoma	III	5/7/7	7.6	5.6	39
17	Undifferentiated carcinoma	II	8/8	55.2	5.0	96
18	Metastasis of an ovarian adenocarcinoma	II	D:5	5.9	1.4	0
		Mean		25.0	3.6	
		Coefficients of variation		0.57	0.63	
Irradiated patients						
15I	Chorion alone with necrosis	III	D:6	5.2	2.9	0
16I	Persistance of few nests of carcinoma altered by radiations	III		7.3	0	1.6
17I	Undifferentiated carcinoma	II	D:8	27.2	3.6	10
19I	Chorion alone with ulceration	III		19.1	4.89	0

[a] Patient 10 received flagyl.

15I: Biopsy 1 month after the end of the irradiation (50 Gy).

16I: Biopsy 4 days after: 20 Gy external,
40 Gy brachytherapy.

17I: Biopsy after 20 Gy (last day).

19I: Biopsy 3 weeks after 20 Gy.

For irradiated cancer patients: a second biopsy was taken from three patients at various times after the end of radiotherapy. The GSH values for Patient 15 before and after irradiation cannot be compared, because the histology of the pre-irradiated and post-irradiated biopsies were different. The quantity of GSH was reduced in Patient 17 after irradiation: a major reduction or complete loss of the tumour was observed. The GSH level was unchanged in the third patient (Patient 16).

For normal tissue: a biopsy of normal tissue was taken from Patients 3, 10 and 11; the GSH contents were 12.9, 24.1 and 24.4 nmol/mg protein while the GSH contents of these patients' tumours were 12.4, 19.8 and 22.8. nmol/mg protein, respectively.

Cysteine content (nmol/mg protein). For non-irradiated cancer patients: the median CYS content was between 4.2 and 4.4 nmol/mg protein (extremes: 0 and 8). No correlation was found between the CYS content and any of the following parameters: tumour size, degree of differentiation, disease stage.

For irradiated cancer patients: the tumour tissue samples from irradiated Patients 16 and 17 had lower CYS contents after irradiation than did the pre-irradiation samples (for Patient 15, see comments on the GSH content). For Patients 3 and 11, CYS contents in normal tissue were 0.77 and 2.8 nmol/mg protein, respectively; these values were lower than those of the malignant tissue biopsies. For Patient 10, the CYS content in normal tissue (1.77 nmol/mg protein) is higher than CYS in malignant biopsy.

Head and neck (Table II).

Biopsies were taken outside the necrotic zones under local anaesthesia. The tumour stage was estimated by the size of the tumour, with three-dimensional measurements wherever possible (TNM classification). Two biopsies were taken in the tumour zone in Patients 10 and 16. The results did not vary with the biopsy site in Patient 10 while some heterogeneity was observed in the biopsies from Patient 16. The GSH contents in the two biopsies in Patient 3 were different although they were taken from two places in the same patient.

Glutathione content (nmol/mg protein). For non-irradiated cancer patients: the median GSH level was 21.9 (extremes: 1.2 and 41.3) for 17 patients. No correlation was found between the GSH level and the tumour stage of the biopsies.

For other patients: the GSH level of Patient 4 increased three-fold after irradiation. The amount of GSH in normal tissue biopsies and in biopsies from three non-cancerous patients (leucoplasia, specific adenitis and severe dysplasia) were almost identical to those of the tumour biopsies.

Cysteine content (nmol/mg protein). The medium CYS content (4.2) found for non-irradiated cancer patients was similar to that found in the cervical cancers, but the range of individual values was greater (extremes: 0 and 21.1). In contrast to the GSH data, the CYS levels in Patient 4 fell after irradiation. The CYS contents of both normal tissue and biopsies from non-cancerous patients were similar to those of tumour biopsies.

Discussion

The GSH contents of biopsies from both cervical and head and neck tumours varied greatly from one patient to another. The mean or median GSH contents for non-irradiated cancer patients are similar to those found for human tumour xenografts (mean $(m) = 24.5$ nmol/mg protein, coefficient of variation $(\sigma/m) = 0.42$; from previous data, Guichard et al, 1986) and lower than those for human tumour cells *in vitro*. The mean GSH content of exponentially growing cells was 39.6 $(\sigma/m = 0.27)$ and that of confluent cells was 39.2 $(\sigma/m = 0.29)$ (unpublished). The GSH content of biopsies from irradiated tumours was never higher than 30 nmol/mg protein for both cervical and head and neck tumours.

The GSH contents of the biopsies taken from non-cancerous patients (head and neck: specific adenitis, leucoplasia and severe dysplasia) were similar to those of normal tissue biopsies from both head and neck and cervix patients.

The CYS levels were three to four times higher than the mean value in only two head and neck tumours; for all the other tumours, the levels were low and certainly no higher than those obtained from the normal tissue biopsies. The variation in the CYS content of tumour biopsies from both cervix and head and neck are greater than those observed for GSH. The variations of CYS are higher than those found for human tumour xenografts $(m = 4.0, \sigma/m = 0.30)$ but not very different from those found for human tumour cells cultured *in vitro* for exponentially growing cells $(m = 6.0; \sigma/m = 0.67)$ and for confluent cells $(m = 4.0; \sigma/m = 1)$ (unpublished results).

The proportion of tumour cells determined from a single histological section can only be approximate. Indeed, there is a certain amount of heterogeneity within a single tumour: thus, when the percentage of tumour cells was studied in four biopsies on four sections, the coefficients of variation were 0.28, 0.31, 0.53 and 0.01. HPLC determination and histological analysis of two segments from a single biopsy indicated that even if tumours are cut in such a way to get the inner, middle and outer region of the tumour in both, the two pieces of biopsy will still not be identical. With these limitations in mind, we looked for a correlation between the GSH level in biopsies and the percentage of tumour in total biopsies (Tables I and II). For head and neck tumours as well as for cervix tumours, the GSH levels in the biopsy does not seem to depend on the proportion of normal cells in the tumour. This is in good agreement with the fact that we obtained similar results when biopsies of normal and tumour tissues were taken from the same patient. Necrosis probably had no decisive influence on the results as it was generally not detected in appreciable amounts. Only the cervical biopsies from Patients 2, 13, 14 and 15 contained significant

Table II. Glutathione and cysteine in head and neck biopsies

Patient	Localization	Histology	Stage	Size (cm)	GSH in nmol/mg protein	CYS	% Tumour in biopsy
Cancer patients (non-irradiated)							
	Oropharynx						
1	Uvula	Squamous cell carcinoma	T3	>10	19.2	4.2	78
2	Uvula		T2	3/4/2	26.3	4.5	80
3	1/2 Soft palate		T2	1.5/4	8.9	1.4	0
4	Hard palate		T3	6/4	10.2	21.1	71
5	Tonsil	Differentiated malignant lymphoma	T3	7/6	20.4	2.8	66
6	Tonsil	Squamous cell carcinoma	T2	2/3	1.2	0	70
7	Ant. faucial pillar		T2	1.5/4	26.3	2.2	2
	Oral cavity						
8	Tongue	Squamous cell carcinoma	T2	3/2	21.4	4.9	87
9	Tongue		T3	Large	23.9	3.0	19
10	Tongue		T3	7/3/2.3	23.1 26.6	4.7 4.2	74
11	Tongue		T3	4/5/2	16.7	4.9	41
12	Tongue		T2	4/2/2	34.4	8.1	38
13	Floor of mouth	Verrucous squamous cell carcinoma	T1	2/1	16.5	3.8	79
14	Floor of mouth	Squamous cell carcinoma	T2	4/4/3	23.3	4.3	97
15	Floor of mouth		T3	6/8/4	41.3	15.3	57
16	Floor of mouth		T2	5/1.5	21.9 31.5	1.9 2.6	15
17	Paranasal cavity	Differentiated adenocarcinona	T3	Large	23.6	4.7	61
			Mean		21.0	5.4	
			Coefficients of variation		0.44	0.99	
Cancer patients (irradiated)							
4[a]	Floor of the maxillary sinus	No tumour			29.7	6.7	0
18[b]	Tongue	Verrucous squamous cell carcinoma	T2	4/2	13.9	2.5	85
Other pathology							
3	Post. buccal region	Severe dysplasia		1/1/0.5	13.5	2.3	0
19[c]	Sub-maxillary lymph node	Specific adenitis		3/2/2	18.8	6.2	0
20	Tongue	Leucoplasia		3/2/0.1	23.2	2.7	0
Normal tissues							
21	Tongue			3/4/2	24.2	3.9	0
22	Post-faucial pillars						
	Left			1/2/1	22.4	1.0	0
	Right				29.6	5.7	
23[d]	Spinal lymph node			2/2/1	19.7	3.2	0

[a] 61.5 Gy 3 months before biopsy.
[b] 80 ± 20 Gy 47 years before biopsy.
[c] Antibiotics 5 days before biopsy.
[d] Antibiotics 1 month before biopsy.

necrotic areas (15% in Patient 2, 11% in Patient 13, 1.4% in Patient 14, 62% in Patient 15). The head and neck biopsy from Patient 6 contained 10% necrosis.

Individual cell thiol contents could not be evaluated by the techniques used in this study. A technique which uses a bimane derivative to estimate GSH in isolated cells shows a five-fold difference in fluorescence intensity between the lowest 1% and the highest 1% of the distribution (Rice et al, 1986). This large difference in fluorescence is a reflection of a considerable heterogeneity of GSH within the cell population. The techniques employed in the present study together with cytofluorimetry using the monochlorobimane marker are not, at present, able to describe the distribution of GSH levels in the oxygenated and hypoxic tumour cells, respectively, which is the major and ultimate objective of any clinical or radiotherapeutic application of these studies.

In conclusion, these data suggest that the mean GSH content of human biopsies from cervix and head and neck is not very high and not higher than in the corresponding normal tissues but there is a wide range of individual values. The variations in CYS content in these biopsies are even greater.

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References

BACQ, Z. M., 1965. *Chemical protection against ionizing radiation* (Ch. Thomas, Springfield), pp. 16–59.

BIAGLOW, J. E., VARNES, M. E., ASTOR, M., MITCHELL, J. & RUSSO, A., 1983. Intracellular thiols: involvement in drug metabolism and radiation response. In *Radioprotectors and Anticarcinogens*, ed. by O. F. Nygaard and M. G. Simic (Academic Press, New York), pp. 203–236.

BROWN, J. M., 1983. Radiosensitizers and radioprotectors: Current status and future prospects. In *Proceedings of the 7th International Congress of Radiation Research: Reviews and Summaries on Chemistry, Physics, Biology, and Medicine*; ed. by J. J. Broerse, G. W. Barendsen, H. B. Kal and A. J. Van der Kogel (Martinus Nijhoff, Netherlands), pp. 281–289.

DISCHE, S., SAUNDERS, M. I., BENNETT, M. H., DUNPHY, E. P., DES ROCHERS, C., STRATFORD, M. R. L., MINCHINTON, A. I. & WARDMAN, P., 1986. A comparison of the tumour concentrations obtainable with misonidazole and Ro 03-8799. *British Journal of Radiology*, *59*, 911–917.

GUICHARD, M., LESPINASSE, F. & MALAISE, E. P., 1986. Influence of buthionine sulfoximine and misonidazole on glutathione level and radiosensitivity of human tumour xenogragfts. *Radiation Research*, *105*, 115–125.

MINCHINTON, A. I., ROJAS, A., SMITH, K. A., SORANSON, J. A., SHRIEVE, D. C., JONES, N. R. & BREMNER, J. C., 1984. Glutathione depletion in tissues after administration of buthionine sulphoximine. *International Journal of Radiation Oncology, Biology, Physics*, *10*, 1261–1264.

ONO, K., KOMURO, C., NISHIDAI, T., SHIBAMOTO, Y., TSUTSUI, K., TAKAHASHI, M. & ABE, M., 1986. Radiosensitizing effect of misonidazole in combination with an inhibitor of glutathione synthesis in murine tumors. *International Journal of Radiation Oncology, Biology, Physics*, *12*, 1661–1666.

REED, D. J., BRODIE, A. E. & MEREDITH, M. J., 1983. Cellular heterogeneity in the status and functions of cysteine and glutathione. In *Functions of Glutathione: Biochemical, Physiological, Toxicological and Clinical Aspects*, ed. by A. Larsson, S. Orrenius, A. Holmgren and B. Mannervik (Raven Press, New York), pp. 39–49.

REVESZ, L. & MALAISE, E. P., 1983. Significance of cellular glutathione in radioprotection and repair of radiation damage. In *Functions of Glutathione: Biochemical, Physiological, Toxicological and Clinical Aspects*, ed. by A. Larsson, S. Orrenius, A. Holmgren and B. Mannervick (Raven Press, New York), pp. 163–171.

RICE, G. C., BUMP, E. A., SCHRIEVE, D. C., LEE, W. & KOVACS, M., 1986. Quantitative analysis of cellular glutathione by flow cytometry utilizing monochlorobimane: some application to radiation and drug resistance *in vitro* and *in vivo*. *Cancer Research*, *46*, 6105–6110.

ROJAS, A., SMITH, K. A., SORANSON, J. A., MINCHINTON, A. I., MIDDLETON, R. W. & DENEKAMP, J., 1984. Enhancement of misonidazole radiosensitization by buthionine sulphoximine. *Radiotherapy and Oncology*, *2*, 325–332.

SEDMAK, J. J. & GROSSBERG, S. E., 1977. A rapid, sensitive and versatile assay for protein using Coomassie brilliant blue G250. *Analytical Biochemistry*, *79*, 544–552.

YU, N. Y. & BROWN, M., 1984. Depletion of glutathione *in vivo* as a method of improving the therapeutic ratio of misonidazole and SR 2508. *International Journal of Radiation Oncology, Biology, Physics*, *10*, 1265–1269.

1990, *The British Journal of Radiology*, *63*, 562–564

Technical notes

Cylindrical forms of isodoses in gynaecological afterloading therapy: an atlas using the Buchler afterloading machine al-mc

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Problems with intravaginal applicators and their solution have outlasted the changes from radium applicators to afterloading techniques. The question of interest is how intravaginal afterloading applicators have to be optimized to take account of unchanged clinical necessities and new technical concepts. According to the recommendations of ICRU 38, the rectal reference point is localized 5 mm behind the dorsal vaginal wall. The reference isodose surface defines the reference volume (ICRU, 1985). It is necessary for the isodoses used in combination with a defined applicator to be adapted to this applicator. While the concept of the "optimized applicator" uses applicators manufactured according to existing isodoses (Lambert, 1988), we progressed to the adaption of the isodoses to existing applicators.

Vaginal applicators

In the radiotherapy department in Göttingen we use vaginal applicators which are cylindrical with a rounded, hemispherical top. From our point of view this form "unfolds" the vagina anatomically without the vaginal walls remaining in contact with each other. Figure 1 represents the attributes of our applicators. The Perspex applicator is cylindrical, available with diameters of 20, 25 and 30 mm. The cylinders are supplied with two copper rings at an interval of 2 cm. The surface of the copper rings is flush with the surface of the Perspex cylinder. From the X-ray film it is possible to identify exactly the applicator as well as the ratio of dimensions. Therefore our vaginal applicator conforms with the applicators developed by Delclos et al (1980) and Perez and Glasgow (1987), and the cylindrical applicators using radium (Marburger Gamma-Applikatoren (Busch & Buchelt, 1973)) and the late devices developed for afterloading techniques (Busch, 1978).

Programmes for isodoses

Using the new afterloading machine al-mc Buchler, it is possible to file and prescribe, in addition to the 50 standard isodoses, another 50 freely defined moving programmes for the source. All filed moving programmes are converted electronically into movements of the iridium source by motors. In this way, mechanical devices with eccentric discs are replaced by steering computers. The Buchler atlas of standard isodoses (Buchler, 1988) consists of linear movement programmes as well as pear-shaped isodose distributions of different length and orientation (Fig. 2). This atlas does not meet all the requirements that are required from an atlas for cylindrical applicators. For that, it has been necessary to calculate a new atlas complying with cylindrical applicators. We have calculated isodoses for cylindrical vaginal applicators using the Buchler afterloading device according to this information. We found the necessary movement programmes for the source empirically, and used the Buchler al-mc computer for the isodose calculations. These isodoses have a cylindrical form at a distance of 5 mm from the surface of the applicator. It has been necessary to allow for every length to be irradiated and each of the applicator diameters in our calculations. This has resulted in individual moving programmes for the iridium source. Thereby the length of the motion of the source varies from 2 cm to 15 cm. The motion of the iridium source generating cylindrical isodoses consists of a linear movement between two stops. Defined cylindrical forms of isodoses demand a definite proportion of dwell time equally shared at the bottom and top of the source movement. The diameter of the Perspex applicator influences the movement programmes in order to guarantee isodose parallel to the surface of the applicator. The isodose with the length of stroke of 40 mm and calculated for a vaginal cylinder with a diameter of 20 mm is demonstrated in Fig. 3. The source stops for 20.5% of the irradiation time at point 1 and for another 20.5% at point 2. The points are 40 mm distant from each other. Between point 1 and point 2 the source oscillates linearly. The result shows an isodose which is parallel at a 5 mm distance from the drawn surface of the applicator.

Table I indicates the defined moving programmes of

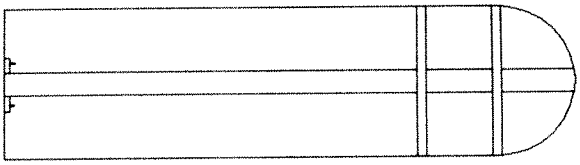
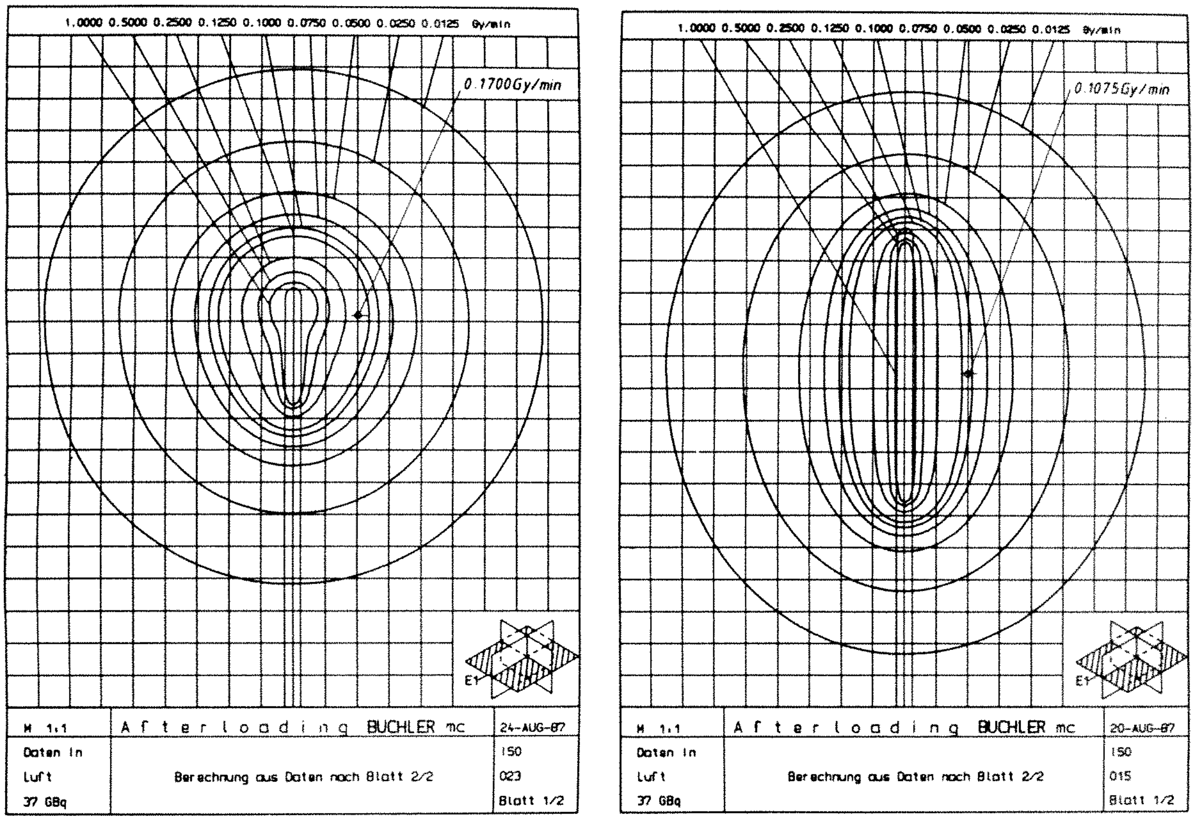


Figure 1. The cylindrical applicator used for vaginal application of the iridium source.



(a) (b)

Figure 2. The Buchler al-mc atlas contains two forms of isodoses, as shown in (a) and (b).

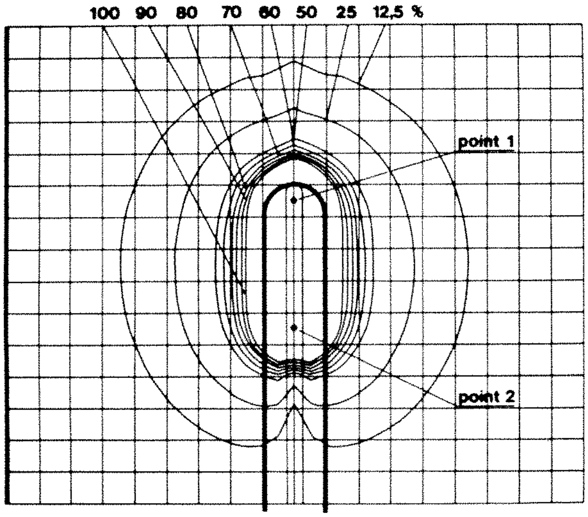


Figure 3. The motion of the iridium source generating the cylindrical isodose consists of linear movement between two stops at point 1 and point 2.

Table I. Percentage dwell times with reference to moving length and vaginal diameter as a percentage of the whole moving time for the iridium source

Length of source movement (mm)	Vaginal diameter		
	30 mm	25 mm	20 mm
20	48.0	48.0	48.0
30	44.0	32.0	27.0
40	24.0	22.0	20.5
50	20.1	19.2	18.5
60	18.5	17.5	15.5
70	16.7	15.4	14.0
80	15.3	14.0	13.0
90	14.2	13.1	12.0
100	13.2	12.2	11.2
110	12.5	11.5	10.5
120	11.8	10.8	9.8
130	11.2	10.3	9.4
140	10.6	9.7	8.9
150	10.2	9.4	8.5

the source. The necessary dwell times are reported with reference to moving length and vaginal diameter. The atlas and the isodose plans can be reconstructed from this table using the Buchler afterloading machine. With this library of isodose programmes we have a new atlas which has been used without any problems at the department of radiotherapy in Göttingen for about 400 gynaecological applications. Because the applicator and isodose are exactly parallel, the organs at risk, "rectum" and "bladder", have never been a cause for complication.

References

BUCHLER, 1988. *Buchler al-mc Standard Isodose Atlas*. (Braunschweig, FRG).

BUSCH, M., 1978. Klinische Applikationsverfahren mit umschlossenen Nukliden. In *Strahlentherapie*, ed. by E. Scherer (Springer, Berlin, Heidelberg), pp. 135–168.

BUSCH, M. & BUCHELT, L., 1973. Optimization of radium sources for vaginal treatment. *Acta Radiologica*, *12*, 263–267.

DELCLOS, L., WHARTON, J. T. & RUTLEDGE, F. N., 1980. Tumors of the vagina and the female urethra. In *Textbook of Radiotherapy*, ed. by G. H. Fletcher (Lea & Febiger, Philadelphia, USA), pp. 812–828.

ICRU, 1985. *Report 38. Dose and Volume Specification for Reporting Intracavitary Therapy in Gynaecology* (ICRU, Bethesda, Maryland, USA), p. 11.

LAMBERT, H. E., 1988. Use of Buchler afterloading machine for carcinoma of the uterus at the Hammersmith Hospital—clinical aspects. In *High Dose Rate Afterloading in the Treatment of Cancer of the Uterus, Breast and Rectum*, ed. by H. Vahrson and G. Rauthe. Supplements to *Strahlentherapie und Onkologie*, *Vol. 82* (Urban & Schwarzenberg, München, FRG), pp. 246–248.

PEREZ, C. A. & GLASGOW, G. P., 1987. Clinical applications of Brachytherapy. In *Principles and Practice of Radiation Oncology*, ed. by C. A. Perez and L. W. Brady (Lippincott, Philadelphia, USA), pp. 252–290.

Quality assurance of viewing boxes: proposal for establishing minimum requirements and results from a Spanish quality control programme

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The Medical Physics Group at the Complutense University of Madrid has undertaken a project, during the last 3 years, under a CEC contract on "Optimization of Radiation Protection in Diagnostic Radiology" (Vañó, 1989) in which a pilot programme of Quality Control (QC) was included (Gonzalez, 1989). Exhaustive patient and occupational dose measurements showed differences between the test results from similar equipment. This fact moved us to set up a Quality Control Programme (Guibelalde & Llorca, 1989), and then several Quality Assurance (QA) programmes.

The necessity to establish minimum performance requirements for image quality, and the convenience of defining objective parameters to make possible further advances in the reduction of patient doses and optimization of image quality, has been pointed out at several Workshops of the Commission of European Communities (CEC) on Image Quality in Diagnostic Radiology. A Working Document of the CEC (1989) has recently been issued emphasizing the need to develop appropriate quality criteria. The aim of these activities is to produce standards and quality criteria that will provide a framework, throughout the European Community, for producing images with minimum patient dose and maximum quality. Efforts to ensure the best quality and consistency of viewing boxes must aid these objectives.

The brightness and uniformity of viewing boxes are two factors that can be measured in absolute units. These factors are not influenced by other elements of image quality control and, therefore, can be used for comparisons between different centres. Furthermore, the measurements can easily be obtained and correlations can be immediately taken to resolve anomalous situations. For these reasons, the quality control of viewing boxes was chosen to be one of the first stages in our QC programme. However, the variety of methods of measurement, their dependence on the light meter used, the vague definition of parameters and poor agreement between real and recommended values in most QA protocols (AAPM, 1978; US Department of Health, 1979; Bäulm, 1982; Gray, 1982; WHO, 1982; Moores, 1987; CEC, 1989) have motivated us to undertake more extensive studies on the measurement criteria.

The diagnostic accuracy of radiology is influenced by the following physical parameters related to the conditions under which the radiologist views the radiographs: room illumination, viewing box brightness (luminance) and uniformity of the viewing box brightness.

Room illumination, the ambient light level in the room, should not be allowed to interfere with diagnosis. The ambient light must be kept low enough to avoid causing reflections off the radiograph, but high enough to prevent dazzling from the viewing box. Luminance is measured with a photometer with or without a diffuser. The physical parameter measured is the illuminance which is defined as the luminous flux per unit surface of the illuminated object. The unit of luminous flux is the lumen (lm). The SI unit for illumination is the lux ($1\ \text{lx} = 1\ \text{lm/m}^2$). Strictly speaking, the illumination only refers to point sources, that is the light source must be far enough away to consider it to be travelling in parallel rays. To measure the room illumination, a photometer was placed at the usual clinical observation distance from the viewing box (about 30 cm) which had been switched off. There is quite good agreement between the recommended values of room illumination found in the literature (Moores, 1987; US Department of Health, 1979). The recommended range is 50–100 lx, which corresponds to the light intensity adequate to evaluate easy visual tasks such as appreciation of highly contrasted details.

A surface emitting or reflecting light produces a sensation of brightness in the eye. The physical parameter associated with brightness is luminance, a measure of the luminous flux emitted per unit projected area from a surface. The unit of luminance is candela per unit area (cd/m^2). Viewing box brightness can be measured using a photometer placed in contact with the surface of the viewing box. The photometer must be calibrated to convert illumination (lx) into brightness (cd/m^2).

For Lambert sources the following relation can be established between the illumination (E) and brightness (B) of a disc of radius r: $E = \pi r^2 B/(r^2 + d^2)$, where d is the distance from the light source to the photometer. This equation is derived for a circular, uniform light disc, but can be reasonably applied to other, near circular geometries. The area of the light source, in this case, is A ($= \pi r^2$). If the photometer is placed in intimate contact with the surface of the light source, the equation becomes: $E = \pi B$ and B will be a measure of the brightness of the source. This latter equation shows the relationship between E (lx) and B (cd/m^2) when the photometer collects all the light emitted from the surface of the source. Hence, π is the calibration factor when a photometer is used with a diffuser, since the diffuser integrates light travelling in various directions. If the photometer does not have a diffuser it collects light travelling in a single direction and there is a direct equivalence between E and B. However, special care must be taken to ensure proper contact between the photometer and the surface of the viewing box. If not, the general equation applies.

The brightness of the whole viewing box could be evaluated if the distance $d \gg r$, the viewing box is then considered as a point source. The conversion becomes: $E = BA/d^2$. In this case, B will be the average brightness of the viewing box which would coincide with the brightness when the photometer is in contact, only if the viewing box has uniform brightness. This conversion formula, although very useful for calibration, is not suitable for practical QA protocols since laboratory conditions must be controlled and the measurements are not obtained quickly.

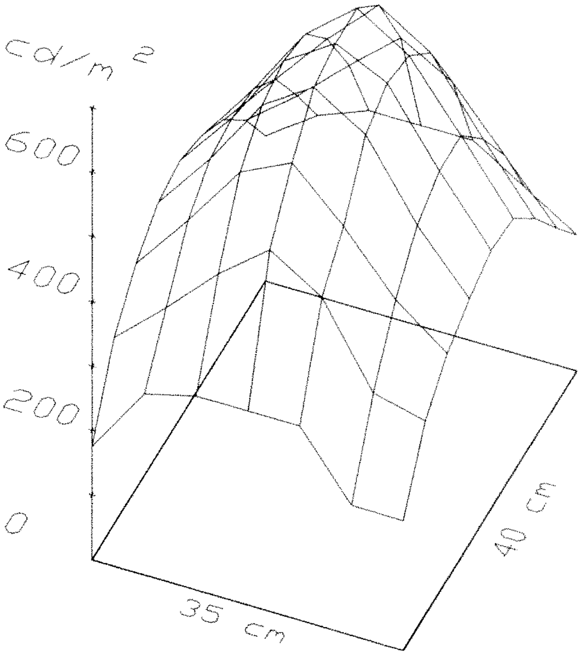

Figure 1. Spatial distribution of brightness at a selected viewing box.

Figure 1 represents the distribution of brightness when the photometer was in contact with the surface of a brand new viewing box. For all measurements a PHYWE 07024.00 photometer with a silicon photocell without diffuser was used. In our case, the conversion equation was: $E = 0.497B$. It is apparent that even for this brand new viewing box, the brightness was not uniform. The brightness has to be clearly established for QA purposes, whether the interest is in the average brightness or the brightness at a particular point. Most authors agree with measuring the brightness at the centre of the viewing box (Bäulm, 1982; Moores, 1987) (our results also refer to the centre), but the uniformity is not so clearly defined. In our QA programme, the non-uniformity of viewing boxes is given by the inhomogeneity, $I = 100\ \sigma(B_N)/B$, where $\sigma(B_N)$ is the standard deviation of the brightness measured at N points (B_N) on the viewing box and B in the mean value of (B_N).

To estimate the number of points and their positions on the viewing box needed to be measured, initially 63 measurements were taken every 5 cm covering the whole of the surface of the viewing box. The inhomogeneity was found to be 50.00% when the whole of the surface was included, and 34.86% when only the central area (or 55% of the total surface) was included. The last result was reproduced with only nine measurements starting at about 5 cm from the edge of the viewing box. This latter technique was employed in the QA programme, knowing that the results could differ if the edges of the viewing box were also considered.

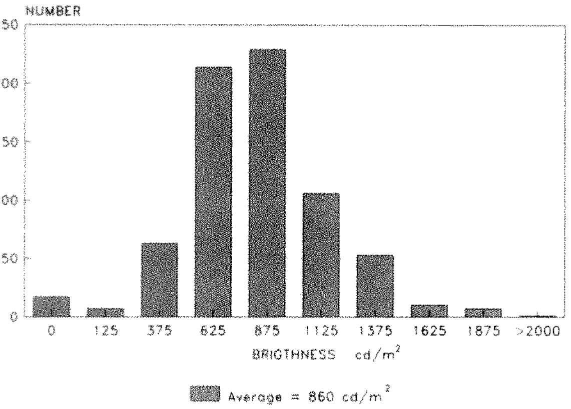

Figure 2. Histogram showing brightness of 707 controlled viewing boxes.

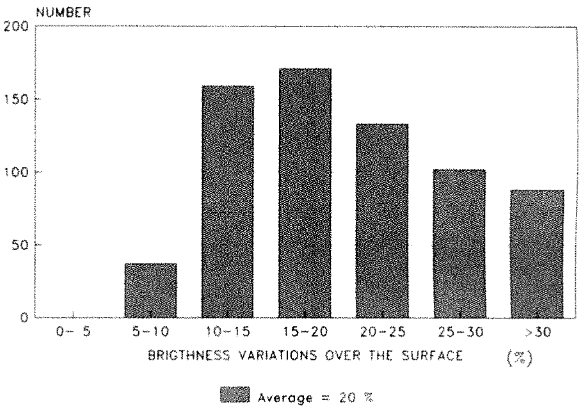

Figure 3. Histogram showing inhomogeneity of the controlled viewing boxes.

The room illumination and the brightness and inhomogeneity of 707 viewing boxes have been measured using the described protocols in four hospitals and two outpatient centres in Madrid. The ambient illumination in all the rooms was within the acceptable limits of 50–100 lx.

A histogram of the brightness of the viewing boxes is given in Fig. 2. High intensity illuminators were not included in this histogram. The mean brightness was 860 cd/m^2 with a standard deviation of ± 295 cd/m^2. Only a small percentage of viewing boxes (4.25%) had brightnesses beyond that considered optimum by some authors (1500 cd/m^2) (Bäulm, 1982; Hartmann, 1989). If 1500 cd/m^2 is to be considered the minimum required brightness, as proposed by the CEC (1989), most of the viewing boxes used at present should be replaced. However, since some of these viewing boxes have less than a year's life-time left, replacing all the viewing boxes that fail the test would not be economical unless the manufacturers can produce viewing boxes giving brightness levels about the 1500 cd/m^2 minimum. This requirement is based on the results of monitoring a number of viewing boxes over a period of 1 year, from which it was deduced that the average annual loss of brightness was 20%.

A histogram of the inhomogeneity of the viewing boxes is shown in Fig. 3. The mean of the inhomogeneity measurements was 20% with a standard deviation of $\pm 10\%$. The results show that 196 viewing boxes (27.72%) have a good uniformity, when applying Hartmann's requirement that the inhomogeneity must be $\leqslant 15\%$ (Hartmann, 1989). If a more restrictive requirement is followed (WHO, 1982; Moores, 1987), namely that the inhomogeneity be $\leqslant 10\%$, only 5.25% of the viewing boxes would comply. Inhomogeneities of greater than 25% have been found in viewing boxes for which the maintenance had not been properly carried out, the inside surfaces had not been cleaned or in which an exhausted fluorescent tube had been replaced without replacing the other tubes in the viewing box, or bank.

These results, which might apply to other Centres where QA programmes are at a similar stage, motivated us to assess the improvement in image quality that will follow the purchase of a new viewing box. For this purpose, images obtained from the Leeds TOR(CDR) test object have been evaluated at different brightness levels. From the image of the spatial resolution test of TOR(CDR), obtained at 50 kVp, a maximum resolution of 8 lp/mm was found for a conventional diagnostic X-ray generator. Figure 4 shows the spatial resolution as a function of brightness level. There was a loss of only 1 lp/mm when the brightness was reduced to 1000 cd/m^2, but the spatial resolution quickly decayed for lower brightness levels.

Similar results were obtained for contrast sensitivity. In this case an exposure of 70 kVp and 1 mm Cu of extra filtration is required to evaluate images from the Leeds TOR(CDR) test object. The variation of contrast sensitivity with brightness is presented in Fig. 5 for large diameter discs with decreasing contrast. Eleven of the 17 discs in TOR(CDR) were visible when the radiograph was viewed at 2500 cd/m^2 (upper curve, Fig. 5). An

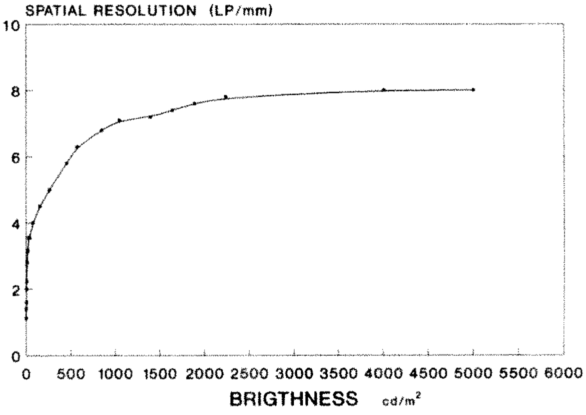

Figure 4. Effect of brightness upon spatial resolution.

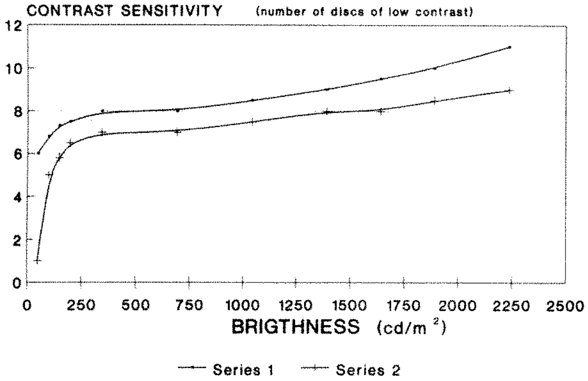

Figure 5. Effect of brightness upon sensitivity contrast of low contrast objects.

almost linear decay in contrast sensitivity was observed for a reduction in brightness from 2500 to 750 cd/m^2. Below 750 cd/m^2, the rate of decay of contrast sensitivity increased. A second X-ray generator was assessed using the same film/screen combination, the same processor, kVp and focus–film distance (lower curve, Fig. 5). It is interesting to note that the decay in contrast sensitivity of this lower curve was more pronounced at insufficient light levels, which implies a poor image quality on the radiograph. Also, to observe eight discs on the second X-ray generator (lower curve, Fig. 5), the brightness would have to be doubled (1500 cd/m^2) relative to the first X-ray generator (upper curve, Fig. 5).

The same is true for Fig. 6 in which the contrast sensitivity *versus* brightness has been plotted for high contrast small discs. Once again, the sensitivity loss was not significant in the range 2500 to 750 cd/m^2, but was significant below 750 cd/m^2. Series 1 and 3 were recorded on the first X-ray generator, with series 3 recorded at half the mAs of series 1. Similarly with series 3 and 4, recorded on the second X-ray generator. These results show that data could be compared to estimate the possible dose reduction achievable when a QA programme is implemented on viewing boxes. Further investigations are to be carried out either using more realistic phantoms, or real radiographs in the near future to complete the data presented in this technical note.

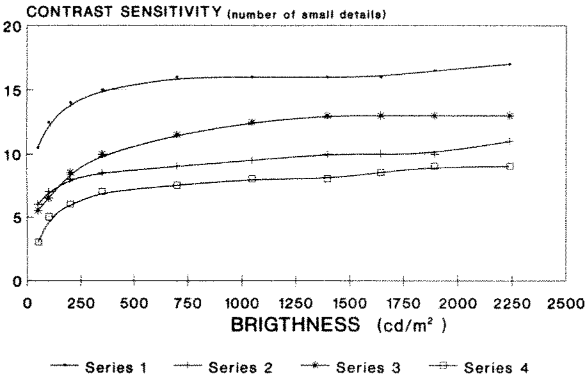

Figure 6. Effect of brightness upon sensitivity contrast of small high contrast objects.

In conclusion, it is proposed that the scientific, technical and administrative communities direct efforts to improve the standards of viewing radiographs. It would be realistic to require the brightness of viewing boxes to be above 1000 cd/m^2, with an inhomogeneity of less than 15% (using definitions presented in this work). More restrictive criteria, *e.g.* above 1500 cd/m^2 with an inhomogeneity below 10%, can be considered as the optimum requirements, but most not be compulsory since the cost *versus* benefit is clearly not justified.

Acknowledgments

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References

AAPM, 1978. *Basic Quality Control in Diagnostic Radiology. Report No. 4* (American Association of Physicists in Medicine, Chicago).

BÄULM, A., 1982. *WHO-Training Workshop on Quality Control and Assurance in Diagnostic Radiologic. Practical Exercises: Film Processing and Viewing Equipment* (Bundesgesundheitsamt. Institut für Strahlenhygiene).

CEC, 1989. *Quality Criteria for Diagnostic Radiographic Images. Working Document XII/108/89* (CEC, Brussels).

GONZALEZ, L., VAÑÓ, E. & GUIBELALDE, E., 1989. Design and preliminary results obtained in a Spanish radiodiagnostic pilot QA program. *CEC DG XII/D/4 International Seminar: Radiation Protection and Quality Assurance in Radiodiagnostic. Madrid, March 1989* (CEC, Brussels).

GRAY, J. E., WINKLER, N. T., STEARS, J. & FRANK, E. D., 1982. *Quality Control in Diagnostic Imaging* (University Park Press, Baltimore).

GUIBELALDE, E. & LLORCA, A. L., 1989. Protocolo de un programa de control de calidad de los soportes de la imagen en Radiodiagnóstico. *Libro de Trabajos VII Congreso Nacional de Física Médica* (Oviedo, Spain).

HARTMANN, E. & STIEVE, F. E., 1989. *Quality Control of Radiographic Illuminators and Associated Viewing Equipment. BIR Report 18* (BIR, London), 135–137.

MOORES, B. M., HENSHAW, E. T., WATKINSON, S. A. & PEARCY, B. J., 1987. *Practical Guide to Quality Assurance in Medical Imaging* (John Wiley & Sons, Chichester).

US DEPARTMENT OF HEALTH, 1979. *Quality Assurance for Radiographic X-ray Units and Associated Equipment. Part 4.11 Uniformity of Radiographic Illuminators. 58. HEW Publication (FDA) 79-8094, Bureau of Radiological Health* (US Government Printing Division, Washington DC).

VAÑÓ, E., GONZALEZ, L., CALZADO, A., MORAN, P. & DELGADO, V., 1989. Some indicative parameters on diagnostic radiology in Spain: first dose estimations. *British Journal of Radiology, 62,* 20–26.

WHO, 1982. *Quality Assurance in Diagnostic Radiology* (World Health Organisation, Geneva).

1990, *The British Journal of Radiology*, *63*, 568–569

Case reports

Intracardiac extension of Wilms' tumour: demonstration by magnetic resonance

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Extension of intravascular tumour thrombus into the right atrium is a well recognized but rare complication of Wilms' tumour (Ritchey et al, 1988). We described the first such case demonstrated by Magnetic Resonance (MR) imaging.

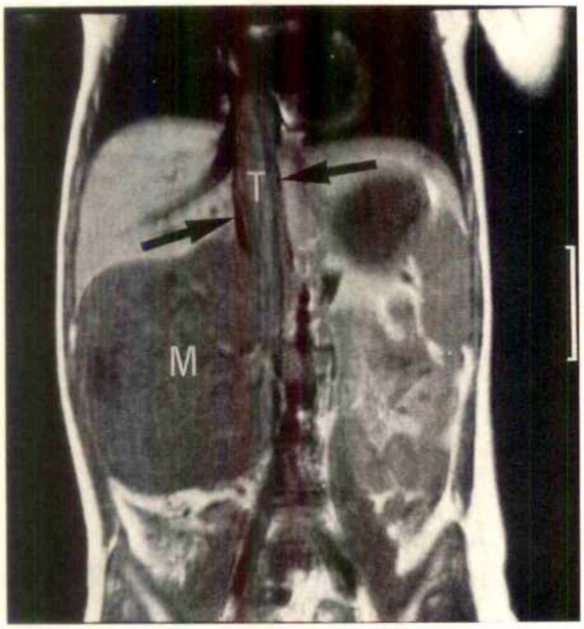

Figure 1. Electrocardiogram triggered, short TR/short TE spin–echo sequence, coronal plane. A large right renal mass (M) is seen with tumour thrombus (T), extending into the IVC and right atrium where it abuts the tricuspid valve. A flow void (arrowed) is seen around the thrombus indicating that it is not adherent to the vessel wall. The signal characteristic of the tumour and thrombus are identical.

Case report

A 5-year-old girl was admitted to hospital with a 1-month history of lethargy and one episode of haematuria. Physical examination revealed a large mass in the right loin and elevation of the jugular venous pressure. Abdominal ultrasound demonstrated a 10 cm echogenic, right renal mass. The inferior vena cava (IVC) was expanded by intraluminal thrombus which extended up to the right atrium. Computerized tomography (CT) confirmed a right renal mass and caval thrombus.

An MR examination was performed on a 1.5T "Magnetom" scanner. Short time to repeat (TR)/short time to echo (TE) spin–echo sequences with electrocardiogram (ECG) triggering were acquired in the sagittal and coronal planes (Fig. 1). Short tau inversion recovery (STIR) sequences ($TR = 3000$ msec, $TI = 150$ msec, $TE = 30$ msec) were acquired in the axial and coronal planes. The findings were:

1. a right sided intrarenal tumour;
2. expansion of the IVC with thrombus extending from the level of the right renal vein, into the right atrium and up to the tricuspid valve;
3. the signal characteristics of the thrombus and primary tumour were identical;
4. a flow void was seen around the periphery of the thrombus suggesting that it was not adherent to the vessel wall.

Echocardiography confirmed intra-atrial tumour, intermittently prolapsing through the tricuspid valve. A combined thoracotomy and laparotomy with cardiopulmonary bypass was performed. Thrombus extended from the right renal vein, into the IVC and right atrium. The primary renal tumour and thrombus were removed "en bloc". Histological examination showed both the primary tumour and thrombus consisted of blastema predominant Wilms' tumour. The renal capsule was intact and lymph nodes were free of tumour.

Nine months later, following systemic chemotherapy, she remains in clinical remission.

Discussion

Although caval thrombus alone does not alter the prognosis in Wilms' tumour (Ritchey et al, 1988) accurate identification is essential to plan treatment and to avoid complications. Unrecognized tumour thrombus has been reported to result in fatal pulmonary embolism in a child with hepatoblastoma (Dorman et al, 1985).

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Antegrade venacavography may be unable to differentiate extrinsic compression of the IVC from intrinsic obstruction; a Valsalva manoeuvre can force contrast medium into collateral vessels and mimic obstruction, and additional retrograde studies may be necessary to delineate the upper extent of any obstruction (Berdon et al, 1967; Slovis et al, 1981). Because venacavography is associated with a risk of dislodging thrombus, a non-invasive method of imaging is preferable. Sonography will show thrombus in the IVC, but in the presence of a large abdominal mass, the IVC may be compressed and difficult to identify. On CT, tumour thrombus in the IVC may be seen as an intraluminal filling defect, or, as in this case, an expanding, non-enhancing mass (Marks et al, 1978). Intravenous contrast medium is required and false positive results have been described resulting from shunting of non-opacified blood through vascular tumours or from layering of contrast medium following bolus injection into the foot vein (Glazer et al, 1981).

Magnetic resonance can identify intravascular thrombus without the use of contrast media, and in this patient showed the intracardiac extent of the thrombus more clearly than either CT or abdominal ultrasound. Comparison of the signal characteristics of the thrombus and primary renal tumour, enables tumour thrombus to be distinguished from blood clot. The presence of a flow void around the thrombus suggests that it is not adherent to or invading the vessel wall.

Magnetic resonance has been reported as a promising imaging technique in patients with Wilms' tumour (Hricak et al, 1985; Belt et al, 1986; Kangerloo et al, 1986). This case illustrates the value in patients with suspected intravascular extension.

References

Belt, T. G., Cohen, M. D., Smith, J. A., Cory, D. A., McKenna, S. & Weetman, R., 1986. MRI of Wilms' tumor: Promise as the primary imaging modality. *American Journal of Roentgenology*, *146*, 955–961.

Berdon, W. E., Baker, D. H. & Santulli, T. V., 1967. Factors producing spurious obstruction of the inferior vena cana in infants and children with abdominal tumors. *Radiology*, *88*, 111–116.

Dorman, F., Sumner, E. & Spitz, L., 1985. Fatal intraoperative tumour embolism in a child with hepatoblastoma. *Anaesthesiology*, *63*, 692–693.

Glazer, G. M., Caller, P. W. & Parker, J. J., 1981. CT diagnosis of tumor in the inferior vena cava; Avoiding the false-positive diagnosis. *American Journal of Roentgenology*, *137*, 1265–1267.

Hricak, H., Demas, B. E., Williams, R. D., McNamara, M. T., Hedgcock, M. W., Amparo, E. G. & Tanagho, E. A., 1985. Magnetic resonance imaging in the diagnosis and staging of renal and perirenal neoplasms. *Radiology*, *154*, 709–715.

Kangerloo, H., Dietrich, R. B., Ehrlich, R. M., Boechat, M. I. & Feig, S. A., 1986. Magnetic Resonance Imaging of Wilms' tumor. *Urology*, *28*, 203–207.

Marks, W. M., Karobkin, M., Callen, P. W. & Kaiser, J. A., 1978. CT diagnosis of tumor thrombosis of the renal vein and inferior vena cava. *American Journal of Roentgenology*, *131*, 843–846.

Ritchey, M. L., Kelalis, P. P., Breslow, N., Offord, K. P., Shochat, S. J. & D'Angio, G. J., 1988. Intracaval and atrial involvement with nephroblastoma: Review of National Wilms' Tumor Study-3. *The Journal of Urology*, *140*, 1113–1118.

Slovis, T. L., Philippart, A. I., Cushing, B., Das, D., Perlmutter, A. D., Reed, J. O., Wilner, H. I., Kroovand, R. L. & Farooki, Z. Q., 1981. Evaluation of the inferior vena cava by sonography and venography in children with renal and hepatic tumors. *Radiology*, *140*, 767–772.

Difficulties in the diagnosis of metastatic testicular teratoma

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Testicular teratoma is the commonest malignancy in men aged 20–30 years. For those with metastatic disease, long term survival used to be exceptional, but with modern chemotherapy 85% will survive 5 years and be considered cured. We report two cases in whom

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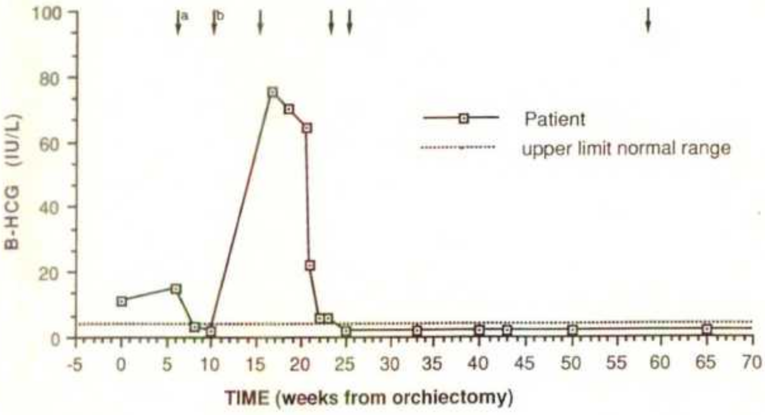


Figure 1. A chart demonstrating the changes in the serum β human chorionic gonadotrophin (βHCG) concentration and the computed tomography (CT) examinations, (↓) in Case 1 (a and b refer to Figs 2a and 2b, respectively).

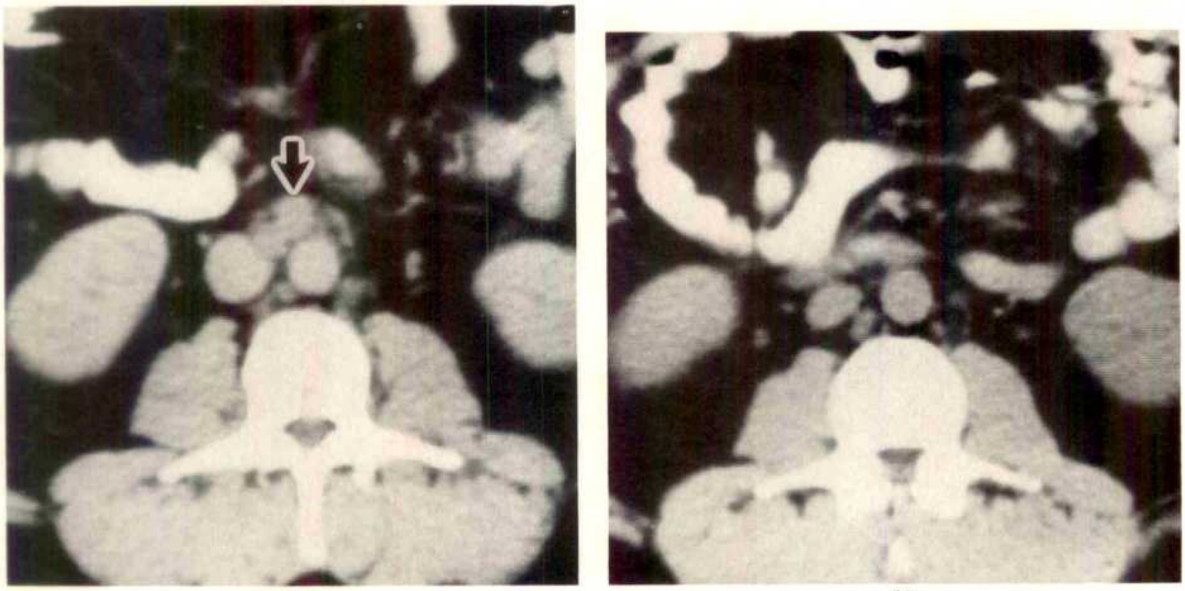
para-aortic lymph node metastases apparently resolved without any systemic therapy.

Case reports

Case 1

A 38-year-old man presented with a 1-year history of painless swelling of the right testis. This had become painful during the month prior to admission. Examination revealed an enlarged right testis but was otherwise normal. He underwent immediate orchdiectomy at which a soft haemorrhagic partially cystic tumour was removed. This proved to be a malignant teratoma (undifferentiated) with lymphatic and venous invasion.

Staging investigations showed a β human chorionic gonadotrophin (βHCG) concentration of 11 IU/l (Fig. 1) and predominantly right-sided para-aortic lymph nodes (Fig. 2a) on abdominal computed tomography (CT). The largest single node was 16 mm in diameter. Because the referral to this centre for cytotoxic chemotherapy was delayed, the CT examination was repeated 4 weeks later to reassess disease extent. This CT study showed that the appearances of the para-aortic region had returned to normal (Fig. 2b). Treatment was deferred and the βHCG concentration returned to normal. Six weeks later the βHCG concentration had risen to 72 IU/l. Therefore CT examinations of head, thorax and abdomen and an ultrasound of the left testis were performed. Although there was no evidence of any new or recurrent tumour on these tests he was admitted for chemotherapy. On admission the βHCG concentration had fallen to 61 IU/l and treatment was deferred again. Serial markers continued to fall to normal levels and CT of thorax and abdomen have remained normal for another 18 months with no treatment.



(a) (b)

Figure 2. *Case 1*. (a) Abnormal nodal material (arrow) in the anterior inter-aorticocaval recess. This magnified image obtained after intravenous enhancement was performed in order to confirm the findings on the original unenhanced series which showed minor nodal abnormalities between the aorta and the cava on several consecutive images. (b) CT scan 4 weeks later showing normal appearances.

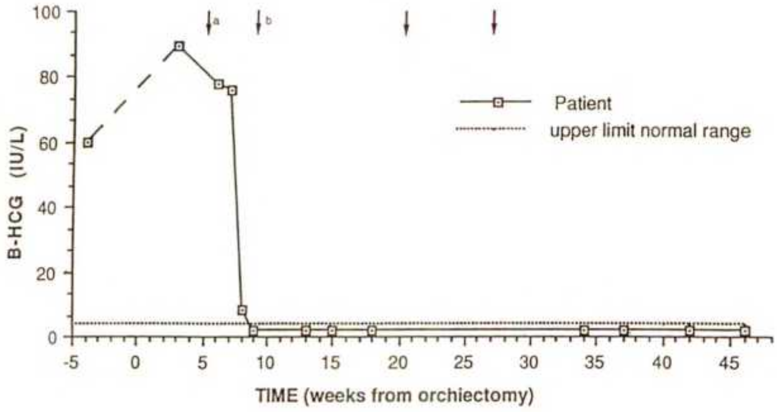


Figure 3. A chart demonstrating the changes in the serum βHCG concentration and the CT examinations (↓) in Case 2 (a and b refer to Figs 4a and 4b, respectively).

Case 2

A 24-year-old man presented with a 1-month history of an aching right testis and lower back pain. On examination there was a hard irregular testis. Pre-operative βHCG concentration was raised (60 IU/l, Fig. 3). Right orchdiectomy was performed and histological assessment of the testis showed malignant teratoma (undifferentiated with yolk sac elements). The tumour had infiltrated through the tunica. He was referred to this centre with persistent back pain and staging CT of thorax and abdomen showed a 5 cm conglomerate mass of para-aortic lymph nodes which engulfed the renal vessels and displaced the duodenum anteriorly (Fig. 4a). The largest individual node measured 2.5 cm in diameter. The βHCG concentration had increased to 89 IU/l (Fig. 3) and a 2 cm supraclavicular lymph node was palpated by three experienced clinicians.

On subsequent admission for cytotoxic chemotherapy the back pain had resolved and the supraclavicular lymph node was impalpable. Repeat tumour markers were normal (βHCG $\leqslant$ 2 IU/l). Chemotherapy was deferred and a second CT examination showed that the nodal mass had resolved (Fig. 4b). Follow-up CT studies have all been normal and he remains in remission 12 months later.

Discussion

The two patients described here were admitted with the intention of administering chemotherapy. Case 1 was first admitted because of the finding of enlarged para-aortic nodes. Repeat CT examination to assess disease progression showed that the nodes had returned to normal. He was subsequently readmitted because of a rise in βHCG level to 72 IU/l. A measurement of βHCG > 60 IU/l was documented on three occasions.

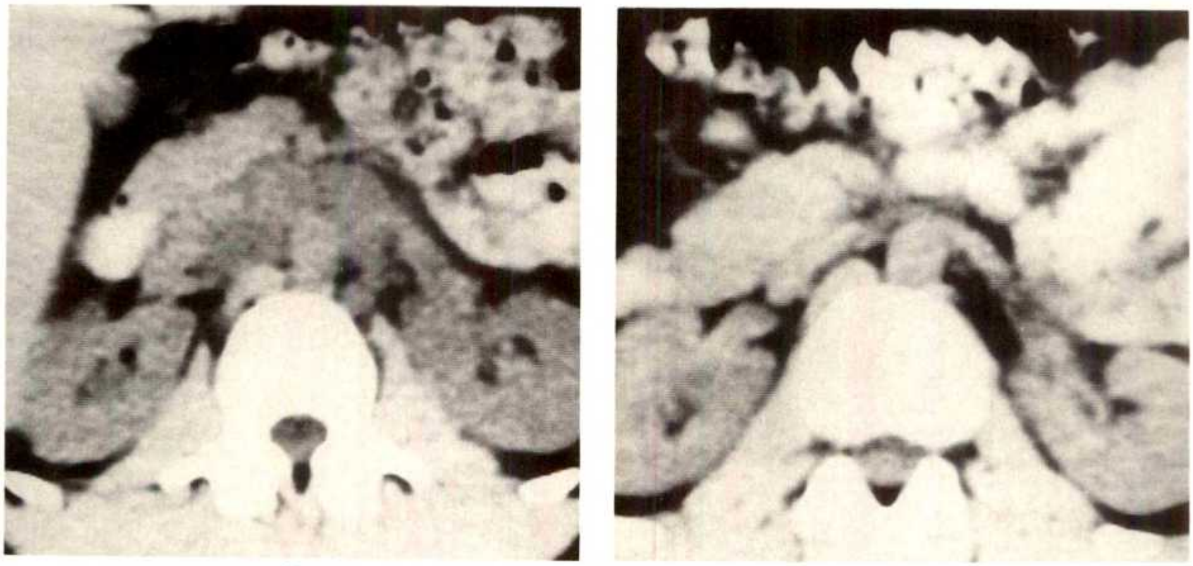

(a) (b)

Figure 4. *Case 2.* (a) Staging CT demonstrating a conglomerate mass of low-attenuation para-aortic nodes engulfing the renal vessels and displacing the duodenum and uncinate process. This mass was at least 5 cm in craniocaudal extent. (b) Complete resolution 4 weeks later.

Such marker-only relapse is considered an indication for chemotherapy (Freedman et al, 1987), but in this case the marker normalized. Case 2 was admitted with an elevated βHCG which had a grossly prolonged marker half life. This is consistent with residual tumour. He also had back pain, a para-aortic mass and a palpable supraclavicular node. Chemotherapy was deferred because of resolution of symptoms and the neck node. The CT appearances and βHCG levels then normalized.

These two cases serve to emphasize the caution which must be used in the diagnosis of metastatic teratoma. The results of chemotherapy are good but treatment related deaths still occur in up to 4% of patients (Williams et al, 1987). In Case 1 radiological and marker abnormalities did *not* coincide and in this situation it may be wise to await definite evidence of progression in such early stage disease. Case 2 showed concurrent symptoms with clinical, radiological and marker abnormalities and would be accepted by many clinicians as having clear-cut metastatic disease. Biopsy proof of metastatic disease is lacking, but spontaneous remission is certainly one explanation of this history; the alternative is an error in diagnosis.

Spontaneous regression in testicular teratoma has been reported sporadically over the last 30 years. Franklin (1977) surveyed 827 cases of whom six had partial or complete spontaneous remission, giving a remission rate of 0.72%. Most previously reported cases have described involution of pulmonary metastases with only few reports of resolution of para-aortic disease. Abdominal CT is now an accepted non-invasive technique for assessing para-aortic node size. Nodes less than 1 cm in diameter are regarded as normal, although micrometastases will escape detection. As in lymphoma, testicular teratoma metastases to lymph nodes tend to result in enlargement (Lee et al, 1979) and it is widely accepted that para-aortic nodes of 2 cm or more in diameter are abnormal (Ellert & Kreel, 1980). Even if the criterion for abnormality is enlargement of nodes to a diameter of 1.5–1.9 cm, the positive predictive value of CT in testicular teratoma is 93% (Lien et al, 1986).

Lymph node enlargement can be seen occasionally in benign conditions. In Case 1 it was considered possible that the enlargement of the right para-aortic node was due to reactive changes following orchiectomy. However, the serum βHCG concentration was abnormal at the time of the CT study and did not finally return to normal for a further 18 weeks. This strongly supports the inference that the enlargement of this particular node, a prime site for right testicular tumours (Dixon et al, 1986) was a result of metastatic involvement.

No treatment other than orchidectomy has been given to these patients. Most of the previously reported cases were given either prophylactic para-aortic radiotherapy (Franklin, 1977) or radiotherapy to symptomatic metastases (Hassenstein, 1977). The mechanism for spontaneous remission is unknown but an endocrinological basis has been postulated (Mueh et al, 1980). Of interest in this context is the observation by Azzopardi et al (1961) that some patients dying of widespread teratoma have only scar tissue at the site of the original tumour. This suggests that the disease may involute in either a local or systemic manner, and a role for immunological surveillance could be postulated.

We conclude that care should be taken to establish the presence of metastatic teratoma on the basis of both radiology and marker elevations. Some metastatic tumours do not secrete markers and in other cases elevated markers may be the only evidence of disease. Nevertheless, if the patient has early stage disease, a period of observation may be wise. Unusual tumour behaviour should raise the possibility of spontaneous remission.

Acknowledgments

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References

Azzopardi, J. G., Mostofi, F. K. & Theiss, E. A., 1961. Lesions of testes observed in certain patients with widespread choriocarcinoma and related tumors. The significance and genesis of hematoxylin-staining bodies in the human testis. *American Journal of Pathology, 38,* 207–225.

Dixon, A. K., Ellis, M. & Sikora, K., 1986. Computed tomography of testicular tumours: Distribution of abdominal lymphadenopathy. *Clinical Radiology, 37,* 519–523.

Ellert, J. & Kreel, L., 1980. The role of computed tomography in the initial staging and subsequent management of the lymphomas. *Journal of Computer Assisted Tomography, 4,* 368–391.

Franklin, C. I. V., 1977. Spontaneous regression of metastases from testicular tumours. A report of six cases from one centre. *Clinical Radiology, 28,* 499–502.

Freedman, L. S., Parkinson, M. C., Jones, W. G., Oliver, R. T. D., Peckham, M. J., Read, G., Newlands, E. S. & Williams, C. J., 1987. Histopathology in the prediction of relapse of patients with stage I testicular teratoma treated by orchidectomy alone. *Lancet, ii,* 294–298.

Hassenstein, E. O. M., 1977. An unusual regression of pulmonary metastases from embryonal carcinoma of the testis. *British Journal of Radiology, 50,* 668–670.

Lee, J. K. T., McClennan, B. L., Stanley, R. J. & Sagel, S. S., 1979. Computed tomography in the staging of testicular neoplasms. *Radiology, 130,* 387–390.

Lien, H. H., Stenwig, A. E., Ous, S. & Fossa, S. D., 1986. Influence of different criteria for abnormal lymph node size on reliability of computed tomography in patients with non-seminomatous testicular tumor. *Acta Radiologica, 27,* 199–203.

Mueh, J. R., Greco, C. M. & Green, M. R., 1980. Spontaneous regression of metastatic testicular carcinoma in a patient with bilateral sequential testicular tumor. *Cancer, 45,* 2908–2912.

Williams, S. D., Birch, R., Einhorn, L. H., Irwin, L., Greco, F. A. & Loehrer, P. J., 1987. Treatment of disseminated germ-cell tumors with cisplatin, bleomycin and either vinblastine or etoposide. *New England Journal of Medicine, 316,* 1435–1440.

1990, *The British Journal of Radiology*, 63, 573–574

Case reports

Cytomegalovirus infection masquerading as colonic neoplasia

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Cytomegalovirus (CMV) infection in the immunocompromized patient usually represents a reactivation of latent infection and occurs in 60–90% of renal transplant patients after initiation of immunosuppressive therapy (Cho et al, 1981). The range of gastrointestinal presentations is wide but a case with the clinical, radiological and operative features of a colonic neoplasm has not previously been described.

Case report

A 53-year-old man was referred with an 8 month history of intermittent epigastric pain associated with diarrhoea for the past 2 months. He had not noticed any blood or mucus in the stools. Nine years previously he had received a cadaveric renal transplant for end stage renal failure secondary to congenital polycystic kidneys. Renal function at presentation was normal on maintenance immunosuppression (Azathioprine 200 mg and Prednisolone 6 mg daily). Physical examination revealed no significant abnormality and full biochemical and haematological investigations were normal.

Endoscopy revealed a normal oesophagus, stomach and duodenum. Ultrasound examination demonstrated multiple hepatic cysts consistent with adult polycystic disease and a mildly enlarged spleen. Both kidneys were absent having been removed prior to transplantation. Sigmoidoscopy was also normal, but a barium enema demonstrated a 5 cm long eccentric stricture involving the proximal transverse colon with mucosal irregularity and ulceration (Fig. 1). The remainder of the large bowel and the distal terminal ileum appeared normal. The differential diagnosis included an atypical colonic adenocarcinoma, lymphoma or even a secondary tumour involving the bowel. The most likely radiological diagnosis, considering the patient's age and clinical presentation, was an ulcerating carcinoma although the appearances were not typical with lack of shouldering and an eccentric position of the stricture.

At surgery, a large irregular mass arising from the proximal transverse colon consistent with the radiological diagnosis was discovered. A right hemicolectomy with end-to-end anastomosis was performed. The patient made an uneventful recovery.

Pathological examination of the resected specimen revealed a stenosing ulcer, 4 × 2 cm in size, 4 cm from the resection line with two smaller shallow ulcers, one 5 cm proximal to the stenosing ulcer and the other adjacent to the ileocaecal valve. Histology revealed multiple nuclear and cytoplasmic inclusions characteristic of CMV with normal intervening mucosa and no evidence of malignancy.

Discussion

Cytomegalovirus infection is now well recognized as an opportunistic infection in the immunocompromized patient. The spectrum of manifestations in the gastrointestinal tract alone is large, ranging from the simple fine ulceration of oesophagitis to the large caecal ulcer presenting with torrential haemorrhage (Rosen et al, 1973; Campbell et al, 1977; Wolfe & Cherry, 1973; Teixidor et al, 1987). Although CMV infection in the immunocompromized has the potential to disseminate with fatal consequences (Nakonecza & Kay, 1967), colonic involvement is usually localized with a predilection for the right side of the colon and in particular the caecum which most commonly presents with severe haemorrhage (Julien et al, 1975; Castaneda-Zuniga et al, 1978; Faro & Corry, 1979; Sutherland et al, 1979). Plaque-like ulcers of varying size, which are the predominant feature of CMV infection in the colon, are best demonstrated at endoscopy because of their typical flat profile and poorly undermined edges. These can be shown on a good-quality double contrast barium enema, but will not always be demonstrated. In this case, the proximal transverse colon was involved and the plaque-like areas of ulceration seen histologically in the ileocaecal area were not visible even retrospectively on the barium enema.

The clinical presentation of this case with a chronic

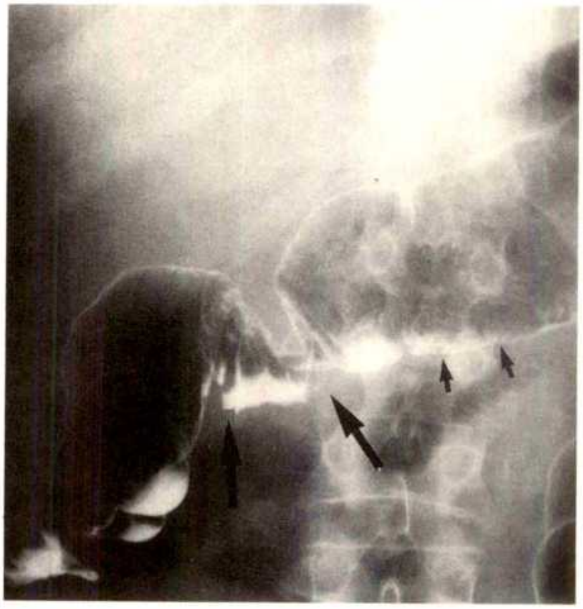

Figure 1. Barium enema showing a slightly eccentric stricture of the proximal transverse colon with mucosal irregularity and ulceration (large arrows) regarded as a carcinoma. The small scattered filling defects (small arrows) in the transverse colon were shown to be faecal.

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history of epigastric pain and mild diarrhoea is most unusual in that all the reported cases of colonic CMV infection presented acutely with either torrential intestinal haemorrhage or a severe colitis and in those patients with renal transplants there was either evidence of severe graft rejection or septicaemic shock. The pathological changes include mucosal ulceration with localized oedema which is partly related to a vasculitis, which may account for the associated haemorrhage and perforation. If these changes are severe, the radiological features of luminal narrowing, thumbprinting, mucosal irregularity and ulceration may suggest a tumour.

It has been suggested that the virus favours infection at sites of endothelial damage. Cases of CMV colitis complicating ulcerative colitis have been reported (Rosen et al, 1973). It may be that steroids, with their potential ulcerogenic effect, could cause the initial endothelial insult which acts as the focus for infection.

This case illustrates that in immunosuppressed patients' cytomegalovirus infection should be included in the differential diagnosis of colonic ulceration and ulcerating strictures which radiologically and clinically may appear to be neoplastic.

References

Campbell, D. A., Piercy, J. R. A., Shnitka, T. K., Goldsand, G., Devine, R. D. O. & Weinstein, W. M., 1977. Cytomegalovirus-associated gastric ulcer. *Gastroenterology*, *72*, 533–535.

Castaneda-Zuniga, W. R., Jaregui, H., Amplatz, K. & Reyes, R. G., 1978. Bleeding from cecal ulcers in renal transplant patients. *Review Interam Radiology*, *3*, 27–31.

Cho, S. R., Tisnado, J., Liu, C. I., Beachley, M. C., Shaw, C. I., Kipreos, B. E. & Shneider, V., 1981. Bleeding cytomegalovirus ulcers of the colon; barium enema and angiography. *American Journal of Roentgenology*, *136*, 1213–1215.

Faro, R. S. & Corry, R. J., 1979. Management of surgical gastrointestinal complications in renal transplant recipients. *Archives of Surgery*, *114*, 310–312.

Julien, P. J., Goldberg, H. I., Margulis, A. R. & Belzer, F., 1975. Gastrointestinal complications following renal transplantation. *Radiology*, *117*, 37–43.

Nakonecza, I. & Kay, S., 1967. Fatal disseminated cytomegalic inclusion disease in an adult presenting with a lesion of the gastrointestinal tract. *American Journal of Clinical Pathology*, *47*, 124–128.

Rosen, P., Armstrong, D. & Rice, N., 1973. Gastrointestinal cytomegalovirus infection. *Archives of Internal Medicine*, *132*, 274–276.

Sutherland, D. E. R., Chan, F. Y., Foucar, E., Simmons, R. L., Hoeard, R. J. & Najarian, J. S., 1979. The bleeding cecal ulcer in transplant patients. *Surgery*, *86*, 386–398.

Teixidor, H. S., Honig, C. L., Norsoph, E., Albert, S., Mouradian, J. A. & Whalen, J. P., 1987. Cytomegalovirus infection of the alimentary canal: Radiologic findings with pathologic correlation. *Radiology*, *163*, 317–323.

Pathological fracture of the femoral shaft in a case of Servelle–Martorell syndrome (phleboeclatic osteohypoplastic angiodysplasia with associated arterio-venous malformation)

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A case is presented of a pathological femoral shaft fracture in a 47-year-old woman with a rare form of skeletal angiodysplasia (Servelle–Martorell syndrome). A simple classification of bony changes in congenital skeletal angiodysplasia is included with a literature review.

Case report

A 47-year-old woman presented to the Accident and Emergency Department having tripped and fallen in the street whilst shopping. The patient had walked with a limp since childhood because of a "short" left leg. A mole had been removed from her left thigh at the age of 9 years. Examination of the left lower limb demonstrated a clinical fracture of the left femoral shaft, 1.5 cm shortening of the left tibia and extensive varicosities with palpable fluid thrill.

Plain radiographs showed a transverse fracture at the junction of proximal and middle thirds of the left femur (Fig. 1). A generalized abnormality was noted in all the bones of the left lower limb (Figs 1 and 2). Pelvic radiographs demonstrated relative hypoplasia of the left hemipelvis. A number of phleboliths were present within the soft tissues of the left lower limb. The early phase of a $^{99}\text{Tc}^{m}$ HDP isotope bone scan showed early venous filling within the left leg, consistent with a significant arterio-venous malformation.

Discussion

Generalized congenital angiodysplasia of the bony skeleton can be divided into four main groups (Table I). In their original paper in 1900, Klippel and Trenaunay described a triad of bony and soft-tissue hypertrophy, haemangiomata and varicose veins. In 1907, Parkes Weber described a similar condition but with additional findings of a thrill transmitted through the venous system consistent with arteriovenous malformation. The term, Klippel–Trenaunay syndrome, is often mistakenly used to include all congenital angiodysplasias without associated arterio-venous malformation, regardless of

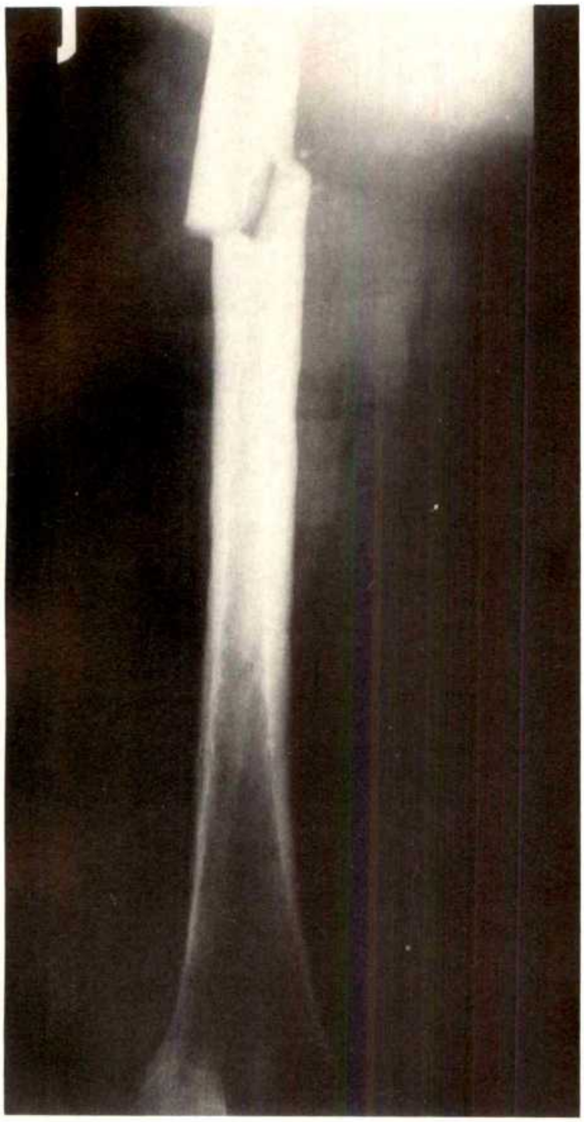

Figure 1. Left femoral shaft demonstrating transverse fracture with irregular, thickened cortex.

whether there is overgrowth, undergrowth or no limb length inequality. Lindenauer (1971) included five cases of congenital short limbs in their series of 25 patients with Klippel–Trenaunay syndrome. Although previously cases attributable to Groups 1 and 3 have been combined as Klippel–Trenaunay syndrome, there would seem to be a case for separating them into cases where the affected limb has shown overgrowth or undergrowth.

The Servelle–Martorell syndrome consists of a phlebectatic osteohypoplastic angiodysplasia with associated arterio-venous malformation producing diffuse permeative lytic changes within affected bones. These changes on plain radiography, and rapid venous filling

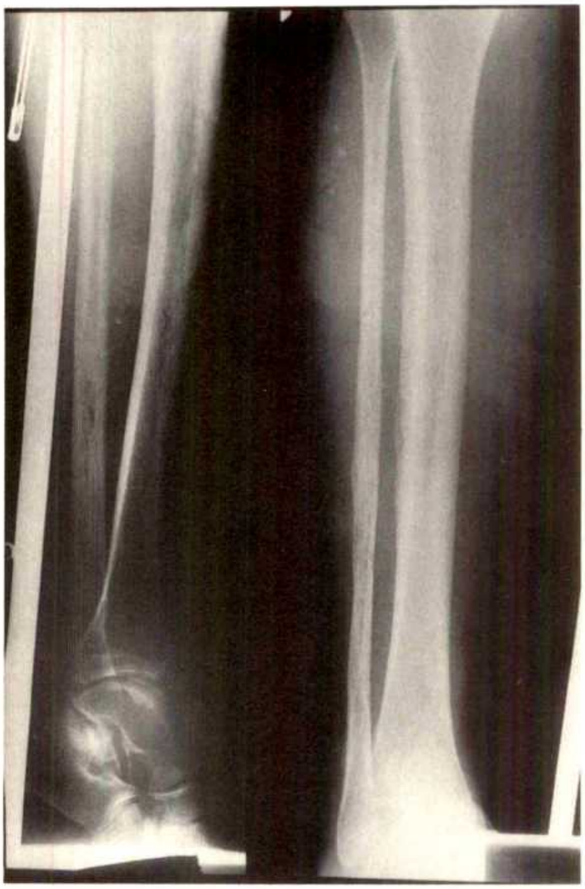

Figure 2. Antero-posterior and lateral left tibia with phleboliths.

during blood pool phase of ^{99}Tc^{m} HDP bone scan or contrast media angiography, allow identification of cases with arterio-venous malformation, *i.e.* types 2 and 4. A number of cases have appeared in the European literature, but this appears to be the first reported case of pathological fracture. The fracture was sustained by minimal indirect force in an otherwise fit and well 47-year-old woman, the angiomatous malformation pre-

Table I. Classification of diffuse congenital angiodysplasias involving the appendicular skeleton

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1 Osteohyperplasia without significant arterio-venous malformation
  (Klippel–Trenaunay type)
2 Osteohyperplasia with arterio-venous malformation involving bone
  (Parkes Weber type)
3 Osteohyperplasia without significant artero-venous malformation
4 Osteohyperplasia with arterio-venous malformation involving bone
  (Servelle–Martorell type)

1990, *The British Journal of Radiology*, *63*, 576–578

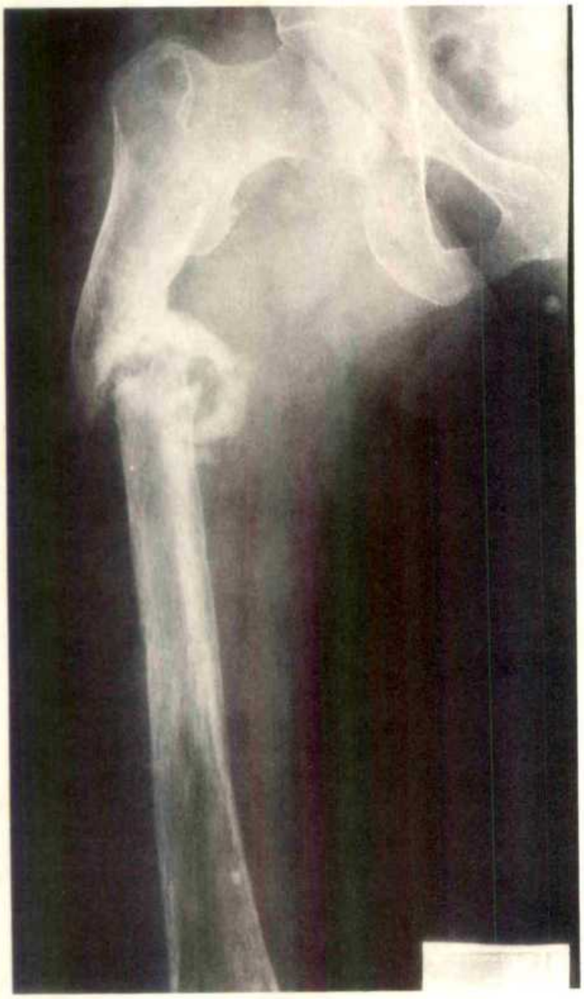

Figure 3. Hypertrophic non-union left proximal femur.

sumably inducing structural weakening of the femoral shaft. In this case the joints are well maintained, although Langer and Langer (1981) described joint destruction in addition to trabecular and cortical bone involvement. Moulin et al (1977) demonstrated a consumptive coagulopathy in their case report of Servelle–Martorell syndrome involving the upper limb.

A further clinical problem related to hypervascularity is the limitation of surgical intervention. An attempt at insertion of a tibial skeletal traction pin in the present case resulted in profuse haemorrhage forcing abandonment of the procedure. The contra-indications to open surgical procedure (Vollmar & Voss, 1978) and inability to control adequately the fracture on skin traction, unfortunately resulted in hypertrophic non-union 18 months after injury (Fig. 3).

References

Klippel, M. & Trenaunay, P., 1900. Du naevus variquex osteohypertrophique. *Archives in General Medicine*, *3*, 641–672.

Langer, M. & Langer, R., 1981. Radiologic analysis of bone structure in congenital angiodysplasia. *European Journal of Radiology*, *1*, 195–199.

Lindenauer, S. M., 1971. Congenital arteriovenous fistula and the Klippel–Trenaunay Syndrome. *Annals of Surgery*, *174*, 248–263.

Martorell, F. & Monserrot, J., 1962. Atresic iliac vein and Klippel–Trenaunay Syndrome. *Angiology*, *13*, 265–267.

Moulin, G., David, B., Bouchet, D., Monier, D. & Lamaud, M., 1977. Angiome veineux ostéohypoplasique géant avec retentissment hémodynamique et coagulopathie. *Annales de Dermatologie et Vénéréologie*, *104*, 479–481.

Parkes Weber, F., 1907. Angioma formation in connection with hypertrophy of limbs and hemi-hypertrophy. *British Journal of Dermatology*, *19*, 231–235.

Servelle, M., 1952. In *Pathologie vasculaire*, *Vol. 1*. (Masson, Paris), pp. 323–329.

Vollmar, J. & Voss, E. U., 1978. Chirugie der kongenitalen angiodysplasen. *Langenbecks Archiv für Chirurgie*, *347*, 255–259.

Epidural abscess of the cervical spine: case report and literature review

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A 51-year-old fisherman with a centro-blastic centrocytic Grade 4B non-Hodgkin's lymphoma only partially responsive to combination chemotherapy over a period of 6 months received an endogenous bone marrow transplant following intensive chemotherapy. His white cell and platelet counts remained low post-operatively, requiring a number of transfusions and continuous antibiotic cover. Two weeks after the transplant he became febrile and developed neck pain which became gradually more severe. Plain radiographs of the cervical spine were normal, as was an isotope bone scan, but the pain continued to increase. A computed tomographic (CT) scan with intravenous contrast medium showed a peripherally enhancing mass within the spinal canal, situated anteriorly between C3 and C6, displacing the thecal sac (Fig. 1). Examination of a sputum sample showed acid-alcohol fast bacilli (AAFB) and, with a provisional diagnosis of an epidural abscess, surgical exploration was undertaken. At laminectomy, no sign of an abscess or granulation tissue could be found, but

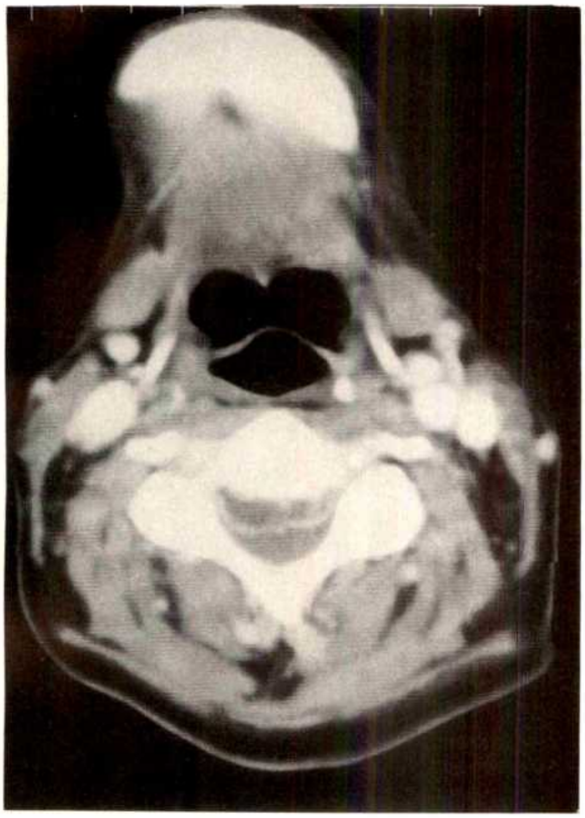

Figure 1. Computed tomographic scan showing a peripherally enhancing mass within the spinal canal, situated anteriorly between C3 and C6, displacing the thecal sac.

post-operatively there was reduced pain and the patient became apyrexial. Ten days later the pain recurred, now associated with weakness of the left arm. Repeat CT revealed a persisting anterior mass (Fig. 2) and CT guided biopsy of the lesion (Fig. 3) yielded approximately 10 ml of thick pus, examination of which confirmed the presence of AAFB.

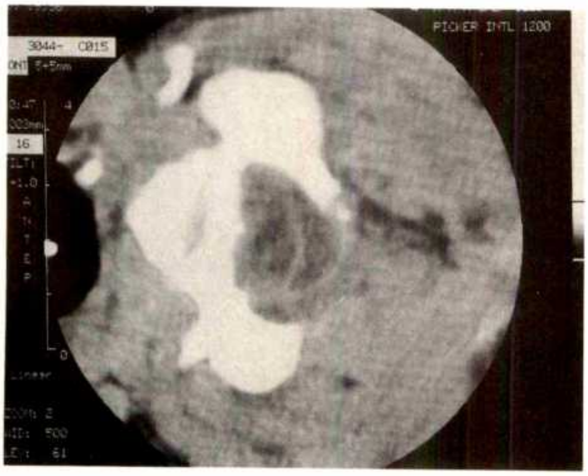

Figure 2. Repeat CT scan showing a persisting anterior mass.

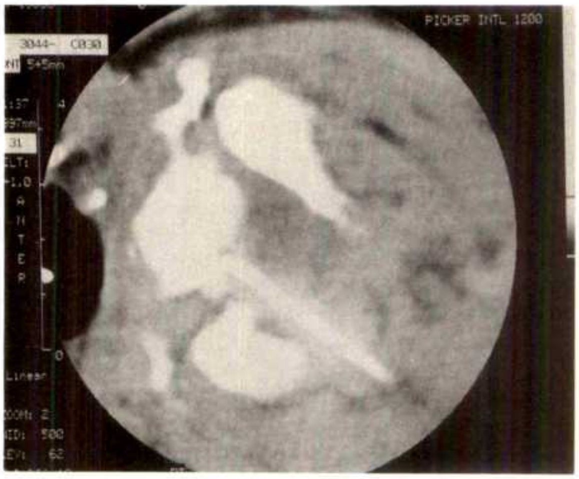

Figure 3. Scan from CT guided biopsy of the lesion.

The patient refused further surgery and, despite antituberculous chemotherapy, rapidly became quadriplegic and later died.

Discussion

Spinal epidural abscess is a rare condition, especially in the cervical spine, forming 12% of 241 cases reported during the antibiotic era (Lasker & Harter, 1987). Cervical epidural abscess is usually associated with osteomyelitis of underlying vertebral bodies, although this may not be detectable at the time of diagnosis.

Delayed diagnosis leads to increased morbidity and mortality from cord compression and venous thrombosis, and septicaemia may occur. Treatment more than 36 h after the development of motor weakness or paralysis is associated with a poor prognosis; in a review of 188 cases of spinal epidural abscess only 39% made a complete recovery (Danner & Hartman, 1987).

Predisposing factors include recent spinal surgery, trauma or instrumentation (a case has been recorded after chemonucleolysis), or by metastatic spread of infection from septic foci in the skin, genitourinary tract or lung. Diabetics, immuno-suppressed patients and intravenous drug abusers are more susceptible.

Twenty-five per cent of cases in the Western hemisphere are a result of tuberculous infection (Werner & Musher, 1985) and are thought to follow reactivation of an old primary focus, which may remain hidden. Most cases are a result of *S. aureus*, although infection by other Gram positive and Gram negative organisms, anaerobes and fungi have been reported (Lasker & Harter, 1987).

Most cases, though not all, have spinal pain at the abscess site. Pyrexia may be absent in chronic cases. Signs of root compression usually appear during the course of the condition. Progression from motor weakness to paraparesis can be rapid. Blood cultures, cerebro-spinal fluid (CSF) examination and erythrocyte sedimentation rate are often informative, but white cell count tends to be unhelpful (Danner & Hartman, 1987).

In the presence of osteomyelitis, plain film abnormalities are found in 82% of cases. Radionuclide bone scans are highly sensitive but lack specificity (Modic et al, 1985).

Myelography has proved extremely reliable in most series and will demonstrate extra-dural compression or a block in almost 100% of cases of epidural abscess, also providing CSF for examination.

Computed tomographic scanning with intravenous or intra-thecal contrast media is a sensitive and informative technique. Using intravenous contrast media, the abscess is shown as a soft-tissue mass with peripheral enhancement replacing the normal fat planes around the thecal sac and displacing it. Gas may be present within the abscess (Kirzner et al, 1988). Osteomyelitis and paravertebral extension can also be recognized and aspiration-biopsy undertaken (Burke & Brant-Zawadski, 1985).

Similarly, magnetic resonance imaging (MRI) can demonstrate the abscess and extensions of the septic process using suitable sequences and differentiate these into liquid content and infectious oedema or granulation tissue; this can be difficult or impossible on CT. Osteomyelitis can be detected with a sensitivity equivalent to that of radionuclide bone scan (Modic et al, 1985; Angtuaco et al, 1987). Following intravenous administration of Gadolinium-DTPA, MRI can define the extent of active inflammation more clearly (Sze, 1988).

Ultrasound has been used intra-operatively to locate an abscess prior to surgical drainage and to assess the adequacy of surgical decompression (Feldenzer et al, 1986).

Conclusion

The optimum treatment of spinal epidural abscess depends on early diagnosis and treatment. The use of enhanced CT and of MRI allows non-invasive diagnosis with the possibility of guided aspiration-biopsy and the instillation of antibiotics prior to surgical, or medical treatment in selected cases (Leys et al, 1985).

References

Angtuaco, E. J. C., McConnell, J. R., Chadduck, W. M. & Flanigan, S., 1987. MR imaging of spinal epidural sepsis. *American Journal of Roentgenology*, *149*, 1249–1253.

Burke, D. R. & Brant-Zawadski, M., 1985. CT of pyogenic spine infection. *Neuroradiology*, *27*, 131–137.

Danner, R. L. & Hartman, B. J., 1987. Update of spinal epidural abscess: 35 cases and review of the literature. *Reviews of Infectious Diseases*, *9*, 265–274.

Feldenzer, J. A., Waters, D. C., Knake, J. E. & Hoff, J. T., 1986. Anterior cervical epidural abscess: the use of intraoperative spinal sonography. *Surgical Neurology*, *25*, 105–108.

Kirzner, H., Youn, K. O. H. & Lee, S. H., 1988. Intraspinal air: A CT finding of epidural abscess. *American Journal of Roentgenology*, *151*, 1217–1218.

Lasker, R. B. & Harter, D. H., 1987. Cervical epidural abscess. *Neurology*, *37*, 1747–1753.

Leys, D., Lesoin, F., Viaud, C., Pasquier, F., Rousseaux, M., Jomin, M. & Petit, H., 1985. Decreased morbidity from acute bacterial spinal epidural abscesses using Computed Tomography and non-surgical treatment in selected patients. *Annals of Neurology*, *17*, 350–355.

Modic, M. T., Feiglin, D. H., Piraino, D. W., Boumphrey, S., Weinstein, M. A., Duchesneau, P. M. & Rehm, S., 1985. Vertebral osteomyelitis: Assessment using MR. *Radiology*, *157*, 157–166.

Sze, G., 1988. Gadolinium-DTPA in spinal disease. *Radiologic Clinics of North America*, *26*, 1009–1024.

Werner, E. F. & Musher, D. M., 1985. Spinal epidural abscess. *Medical Clinics of North America*, *69*, 375–384.

Primary osteosarcoma of the uterus

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Post-menopausal vaginal bleeding is a common clinical problem. Often, the clinician will call upon the radiologist to perform and interpret studies such as ultrasound or computed tomography (CT), to aid in the diagnosis or to evaluate further a pelvic mass. The following case illustrates an unusual cause of post-menopausal vaginal bleeding, with ultrasound and CT images of the pelvic mass. Certainly, the radiologist, in interpreting scans and correlating them with clinical data, must always consider common etiologies first; but one must also remember the uncommon and even rare entities that may radiologically mimic a more common pathologic process and, if appropriate, might be included in the differential diagnosis.

Case report

The patient was a 58-year-old gravida 0, para 0, white woman who presented with a history of progressively worsen-

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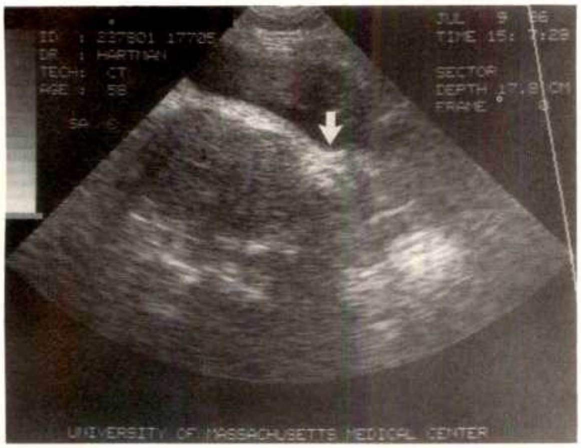

Figure 1. Sagittal ultrasound image showing the echogenic lower uterine segment mass (arrow).

ing post-menopausal vaginal bleeding. Vaginal examination revealed an intact hymenal ring and an irregular, nodular cervix protruding into the upper third of the vagina, which had nodularity of its fornices and walls. Bimanual examination was difficult; the adnexae could not be adequately evaluated. Laboratory data revealed the patient to be anaemic, with a haemoglobin of 3.4 gm at the time of initial presentation.

Pelvic ultrasound revealed an 8 × 8 × 6 cm uterine mass involving the lower uterine segment and causing an extrinsic mass impression upon the posterior wall of the urinary bladder. Bright echoes with acoustic shadowings, interpreted as from calcifications, were identified within the mass, particularly in the cervical segment. The adnexae were not well demonstrated, and no free pelvic fluid was identified (Fig. 1).

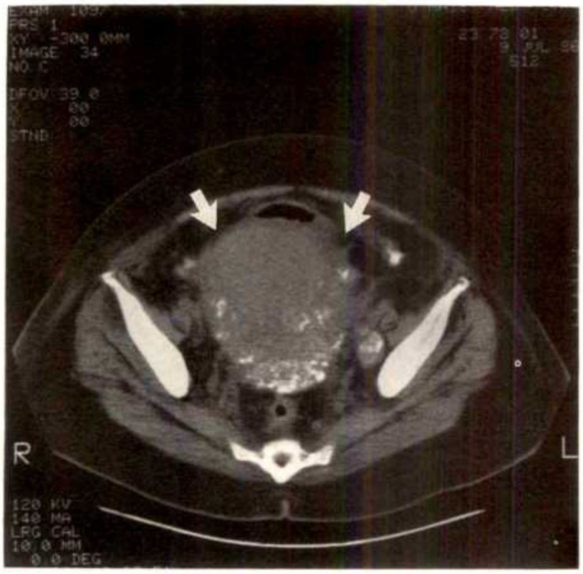

Figure 2. Computed tomographic scan image showing the uterine mass (arrows) with calcification.

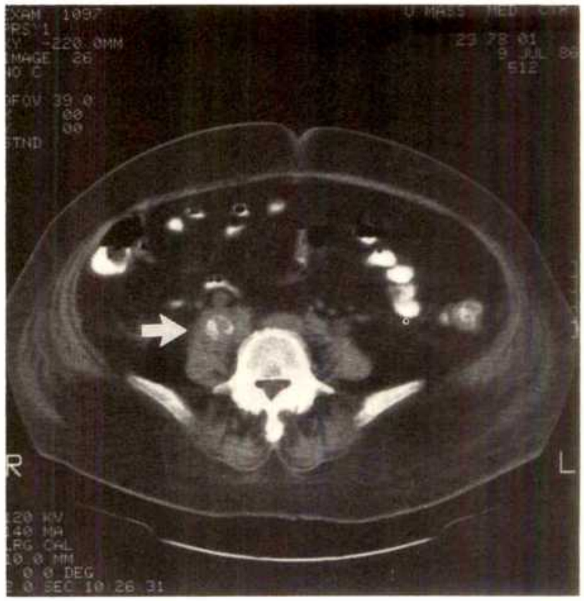

Figure 3. Computed tomographic scan image showing calcification in the right psoas muscle (arrow).

A CT scan the same day showed a 6 × 8 × 10 cm pelvic mass contiguous with the uterus, with calcification and a central area of low attenuation (Fig. 2). A circular calcification within the right psoas muscle was also identified (Fig. 3). No adenopathy was seen. The liver and spleen appeared normal. No free fluid was identified.

Approximately 3 weeks after the initial presentation, examination under anaesthesia and biopsy of the cervix and vagina were performed, but the patient refused further surgical intervention. These biopsies were interpreted as sarcoma with osteoid and bone formation. Following a discussion with the

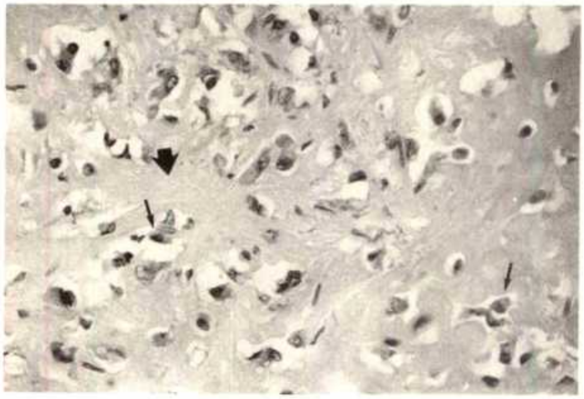

Figure 4. Photomicrograph of the tumour in the uterus showing disorganized and malignant cells (small arrows) surrounded by osteoid formation (large arrow). The tumour cells are pleiomorphic and irregular and are arranged in a haphazard fashion. This malignant osteoid is diagnostic for osteogenic sarcoma. (H & E, × 400.)

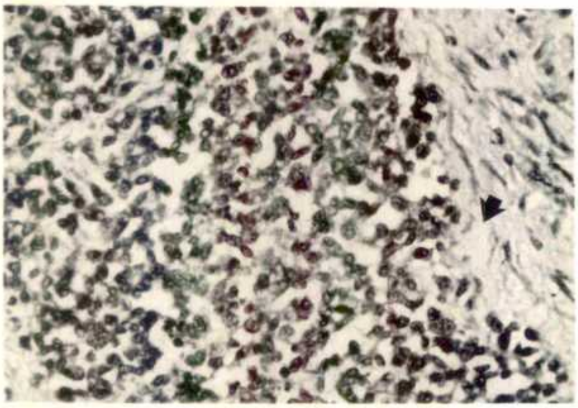

Figure 5. A second pattern of tumour growth is seen in both the primary tumour and the metastases. Portions of the mass are composed of small hyperchromatic anaplastic cells growing in sheets between areas of malignant osteoid (arrow). These anaplastic cells are the dedifferentiated portion of the osteogenic sarcoma. (H & E, ×400.)

patient and her family, a decision was made to provide the patient with supportive measures only, and she died 2 weeks later.

At autopsy, the uterus was markedly enlarged and disorted with a globular shape measuring 18 × 7 × 6 cm. This mass was rock-hard, covered by serosa, and extended to the urinary bladder, anterior wall of the rectum, cervix, and upper two-thirds of the vagina. Both ureters were encased in tumour at the vesicular-ureteral junction, with resulting bilateral hydronephrosis. The uterine cavity was totally obliterated by the bony neoplasm. The ovaries and tubes were adherent to the uterine mass. Metastatic tumour was seen in the peritoneal surfaces, para-aortic lymph nodes, omentum, liver and lungs. No tumour of the skeletal system was found.

A specimen radiograph obtained at the time of autopsy revealed the large uterine mass with calcification involving the cervix and proximal vagina. The right psoas metastasis was also identified.

Microscopically, the tumour consisted of small cells with scant cytoplasm, moderate pleomorphism, nuclear folds, and prominent nucleoli (Figs 4 and 5). Extensive osteoid with calcification was present in the areas of the tumour cells. Examination by polarized light demonstrated dense collagen characteristic of osteoid arranged haphazardly around tumour cells and between smooth muscle cells of the myometrium. No evidence of epithelial differentiation or differentiation along other mesenchymal cell lines was found. The metastatic deposit in the right psoas muscle showed the same morphology as the primary tumour with intervening bands of striated muscle. The final diagnosis was sarcoma of the uterus with osteoid and bone formation consistent with osteosarcoma, fulfilling the criteria set by Piscioli et al (1985) for the diagnosis of pure osteosarcoma of the uterus.

Discussion

Pure primary osteosarcoma of the uterus is a rare entity, with eight previously reported cases in the literature (Crum et al, 1980; Vakiani et al, 1982; Jotkowitz & Valentine, 1985; Piscioli et al, 1985). Seven of the eight patients (Crum et al, 1980; Jotkowitz & Valentine, 1985; Piscioli et al, 1985) and our reported patient were post-menopausal. The most frequent presenting symptom is abnormal or post-menopausal vaginal bleeding (Crum et al, 1980; Piscioli et al, 1985). Physical examination frequently reveals a large, firm uterine mass. Radiography of each of the previously reported cases is not available, but the case reported by Jotkowitz and Valentine had an extensive radiological evaluation prior to surgery. In that case, plain films revealed a large calcified pelvic mass, as well as areas of calcification anterior to the lumbar spine in the para-aortic region and in the left iliac fossa. Intravenous urography and barium enema confirmed the presence of a large pelvic mass but did not add to the diagnosis. Computed tomography revealed a large pelvic mass in the expected location of the uterus containing an annular ring of calcification and a calcified core. They described zones of peritoneal calcification especially to the left of midline and calcification along the common iliac lymph node chain, as well as in the para-aortic and pericaval lymph node groups (Jotkowitz & Valentine, 1985).

Despite surgical intervention, chemotherapy and radiation therapy, the prognosis is poor, with an average survival of approximately 5 months following the diagnosis (Crum et al, 1980; Vakiani et al, 1982; Jotkowitz & Valentine, 1985; Piscioli et al, 1985).

In most cases, this large, calcified uterine mass would be diagnosed as a uterine leiomyoma, or perhaps as a leiomyosarcoma, in the appropriate setting. The most obvious clue to the radiologist that this mass represented a more bizarre entity was the calcified metastasis within the right psoas muscle. Another clue to the diagnosis was the spiculated "trabecular" pattern of the calcification within the mass. Correlation of the images, revealing a large uterine mass containing bone and evidence of bony metastasis, with the clinical information that the patient is post-menopausal, presenting with vaginal bleeding, and has a very firm uterine mass, allows the radiologist to consider the diagnosis of primary osteogenic sarcoma.

References

Crum, C. P., Rogers, B. H. & Andersen, W., 1980. Osteosarcoma of the uterus: Case report and review of the literature. *Gynecological Oncology, 9,* 256–268.

Jotkowitz, M. & Valentine, R., 1985. A rare pelvic mass: Osteosarcoma of the body of the uterus. *Australian and New Zealand Journal of Obstetrics and Gynaecology, 25,* 132–136.

Piscioli, F., Govoni, E., Polla, E., Pusiol, T., Dalri, P. & Antolini, M., 1985. Primary osteosarcoma of the uterine corpus. Report of a case and critical review of the literature. *International Journal of Gynaecology and Obstetrics, 23,* 377–385.

Vakiani, M., Mawad, J. & Talerman, A., 1982. Heterologous sarcoma of the uterus. *International Journal of Gynecological Pathology, 1,* 211–219.

1990, *The British Journal of Radiology*, *63*, 581–582

Case of the month

Just another case of varicose veins?

By R. C. Travis, FRCR, *D. M. Rowan, FACD and J. Miller

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(*Received May 1989 and in revised form August 1989*)

A 49-year-old Maori woman was referred to the Surgical Outpatients Department because of increasing discomfort and disability in the left leg. She had varicose vein surgery as a child, and the veins later recurred. Views from her left lower limb venogram and bilateral aorto-femoral angiogram are shown.

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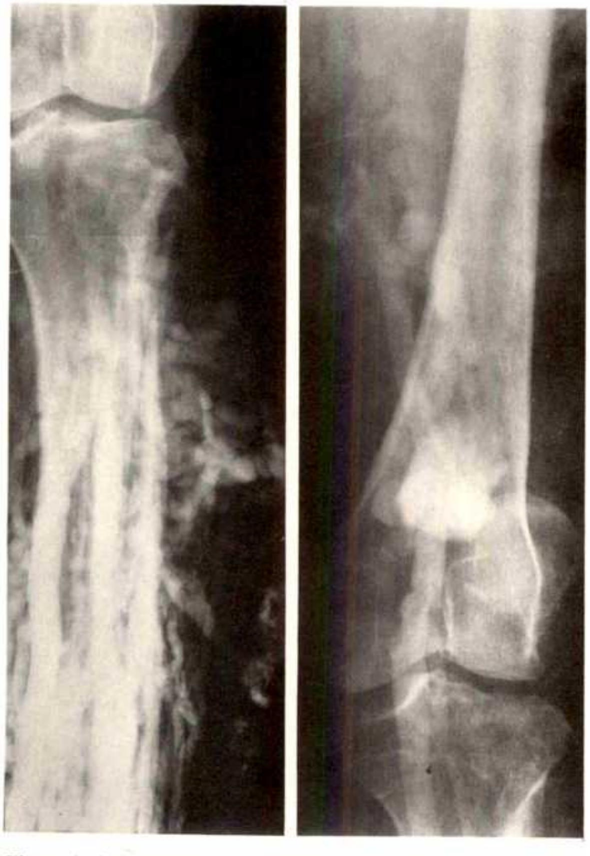

Figure 1. Antero-posterior views from the left leg venogram.

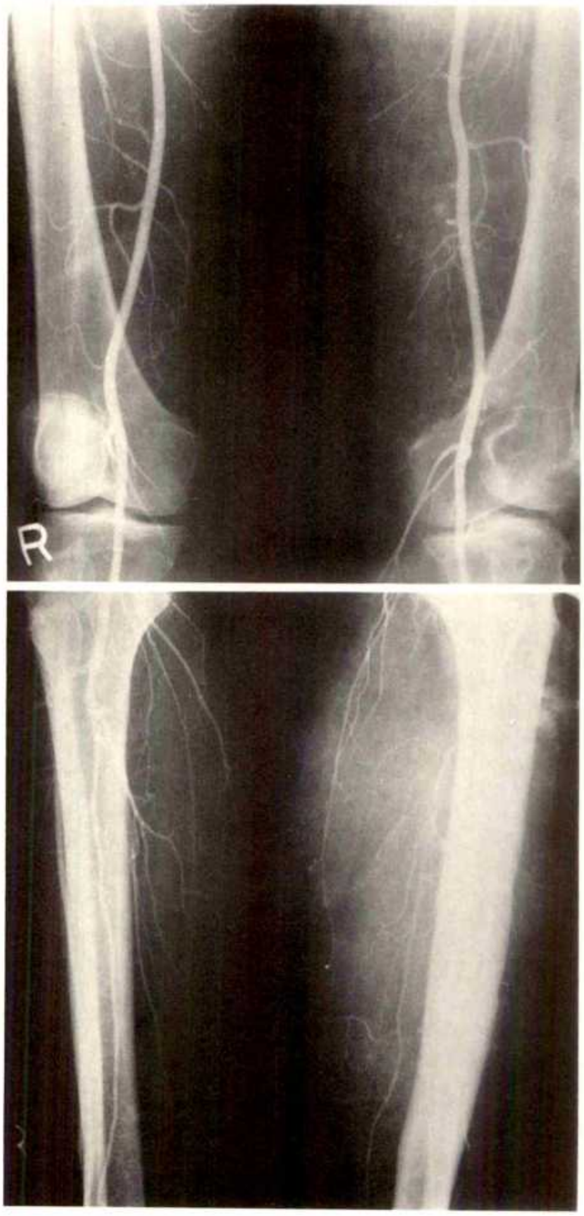

Figure 2. Views from the lower limb arteriogram.

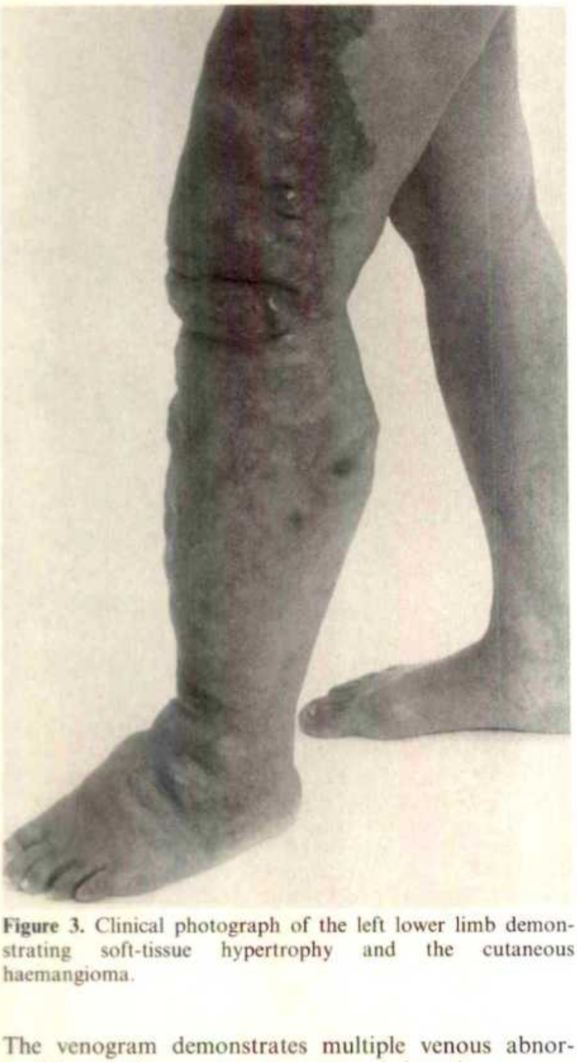

Figure 3. Clinical photograph of the left lower limb demonstrating soft-tissue hypertrophy and the cutaneous haemangioma.

The venogram demonstrates multiple venous abnormalities. Varicose veins are seen and there is a venous aneurysm at the level of the left knee. Thrombus is present in the superficial veins. The deep veins appear patent. The angiogram shows cortical thickening of the tibia and soft-tissue hypertrophy, together with multiple small vascular malformations in the left leg. No arteriovenous shunt was seen. On clinical examination, there was a classical port wine stain (Fig. 3) and lengthening and soft-tissue hypertrophy of the left leg.

Discussion

The patient has Klippel–Trenaunay Syndrome (KTS). This was first described in 1900 by two French physicians, Klippel and Trenaunay as the "naevus variqueux osteo-hypertrophique" syndrome. The clinical manifestations are usually monomelic, and consist of venous varicosities, a port wine haemangioma and bone and soft-tissue hypertrophy of the affected limb (Taybi, 1983). Parkes-Weber described a similar syndrome in 1907 seen in association with a arteriovenous fistula. It is generally accepted that in KTS there is no clinically apparent or angiographic arteriovenous fistula (Lindenauer, 1971). Cases that have a significant arteriovenous fistula tend to be classified as Klippel–Trenaunay–Weber Syndrome.

A mesodermal defect which involves angiogenesis in the primitive limb bud has been postulated as a cause for KTS (Baskerville et al, 1985a). It is thought that late regression of the vascular reticular network causes persisting arteriovenous connections and venous abnormalities. There are no known hereditary factors, and no sex predeliction.

The syndrome presents at birth with the port wine nevus. The varicose veins become more prominent when the child begins to stand erect. Limb hypertrophy may be gross at birth or may become more noticeable at puberty with the growth spurt. Multiple venous abnormalities are usually present. There may be hypoplasia or aplasia of the deep venous system. A valveless lateral venous channel can be seen in the leg which drains into the pelvic veins, and accompanies the sciatic nerve. Varicosities can be seen in the peroneal and supra-pubic areas, and may involve bladder, colon and uterus. The pelvic varicosities can contain phleboliths. Patients may present with haematuria, rectal blood loss or menorrhagia (Azouz, 1983). Superficial thrombophlebitis is not uncommon. Some authors report a high incidence of pulmonary embolus (Baskerville et al, 1985b).

The manifestations tend to progress until the end of the third decade. Surgery may be indicated for troublesome superficial varicosities. However, generally it should be avoided and only attempted after careful venography. Incisions through the cutaneous haemangioma tend to heal poorly. Epiphysiodesis can be used to correct the leg length discrepancy. Most patients can be managed successfully with elastic stockings. Symptomatic haemodynamically significant arteriovenous malformations may be amenable to embolotherapy.

References

Azouz, E. M., 1983. Hematuria, rectal bleeding and pelvic phleboliths in children with the Klippel–Trenaunay Syndrome. *Pediatric Radiology, 13,* 82–88.

Baskerville, P. A., Ackroyd, J. S. & Browse, N. L., 1985a. The etiology of the Klippel–Trenaunay Syndrome. *Annals of Surgery, 202,* 624–627.

Baskerville, P. A., Ackroyd, J. S., Lea Thomas, M. & Browse, N. L., 1985b. The Klippel–Trenaunay Syndrome: clinical, radiological and hemodynamic features and management. *British Journal of Surgery, 72,* 232–236.

Lindenauer, S. M., 1971. Congenital arteriovenous fistula and the Klippel–Trenaunay Syndrome. *Annals of Surgery, 174,* 248–263.

Parkes-Weber, F., 1907. Angioma formation in connection with hypertrophy of limbs and hemihypertrophy. *British Journal of Dermatology, 19,* 231–235.

Taybi, H., 1983. *Radiology of Syndromes and Metabolic Disorders* (Year Book Medical Publishers, Chicago), p. 210.

1990, *The British Journal of Radiology*, *63*, 583–584

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(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Dysphagia after fast neutron therapy to head and neck

THE EDITOR—SIR.

The paper "Dysphagia after fast neutron therapy to the head and neck" by Alexander et al (1989) is most interesting. It is important, not only as a valuable account of late radiation damage following neutron therapy, but also in providing further evidence of the high incidence of serious late complications observed in the patients treated in the studies conducted at the MRC Cyclotron Unit. Very few of these patients were long-term survivors and so the number at risk for late complications was correspondingly small. The Hammersmith studies, for this reason, may have seriously underestimated the late morbidity from neutron therapy. Actuarial calculation of the rates for late complications offers a partial solution to this problem.

Current trials of neutron therapy (RTOG, MRC) use dose/time treatment schedules similar to those used at Hammersmith, but include fitter patients with less advanced tumours. These patients are consequently more likely to survive long enough to develop late complications. To provide essential guidance for these studies we need to have reliable data on the late complications of neutron therapy. The MRC Neutron Therapy Committee would be well advised to commission a review of all long-term survivors to determine actuarially the incidence of serious late complications observed in these patients following neutron therapy.

Clinical investigators involved in the ongoing experimental evaluation of fast neutron therapy require these data. The information should also be available to physicians and surgeons who may refer patients for inclusion in fast neutron therapy trials using similar techniques and doses to those reported in this paper.

Yours, etc.,
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Reference

ALEXANDER, M. S. M., EDELMAN, G. M., MAN, K. & RANDALL, 1989. Dysphagia after fast neutron therapy to the head and neck. *British Journal of Radiology*, *62*, 724–728.

Intraluminal irradiation in oesophageal tumours using the high-dose-rate Microselectron

THE EDITOR—SIR.

We were interested to read the technique for intraluminal irradiation of oesphageal tumours described by Burt and his colleagues (1989) and wish to comment on the conclusions that they have drawn from their limited experience with the high-dose-rate Microselectron.

Since January 1985 we have used intraluminal radiotherapy as part of the treatment of more than 300 patients with either oesophageal or cardia tumours. These patients represent more than 90% of all the patients with oesphageal tumours referred to our centre. Our only contra-indications to intra-oesophageal brachytherapy in previously untreated patients are those to any form of radiotherapy—such as a tracheo-oesophageal fistula. We do not routinely use intra-oesophageal treatment when the majority of the tumour is extraluminal, as is often the case in patients with recurrence following oesophagectomy.

The first 260 patients were treated with the medium/low-dose-rate Selectron (Flores et al, 1987), the last 44 patients have been treated with the high-dose-rate Microselectron. The high-dose-rate machine offers certain advantages, in particular a greater range of treatment positions for the source and shorter treatment times. These two features combine to make it feasible to treat longer tumours in a more acceptable time than was possible with the medium/low-dose-rate machine. The possibility of insertion via the nasal, rather than oral, route makes it possible to intubate the very small minority of patients who are unable to tolerate oral intubation. We have found that the actual intubation techniques required for the different applicators for the two machines are very similar.

Burt et al claim that the standard 6 mm oesophageal applicator supplied with the high dose rate Microselectron "requires oesophagoscopy for insertion and the placement of a guide wire through the tumour over which the applicator is threaded". This is not the case; in fact, we have not used osophagoscopy in any of the patients that we have treated. We do advocate insertion over a guide wire because the tips of both the 6 mm and 8 mm applicators are hard and the applicator tubes are relatively rigid as is the deep frozen 14 gauge nasogastric tube that Burt recommends. We feel that insertion over a guide wire reduces the risk of oesophageal perforation and we have not had any clinically apparent oesophageal perforations in this group of patients. In order to make it more comfortable for the patient, we pass the guide wire in an 8 gauge nasogastric tube from which the distal 10 cm have been removed, the tube is usually inserted through the mouth, but can be passed through the nose. This allows us to manipulate the wire through the tip of the nasogastric tube without irritating the patient's mouth or throat and ultimately to remove the tube prior to inserting the oesophageal applicator along the guide wire.

We do not recommend that radio-opaque contrast medium is given at the time of oesophageal intubation for three reasons. First, the risk of tracheal aspiration is high in patients who have received topical pharyngeal and nasopharyngeal anaesthetic. Burt et al recognize this because after giving the contrast medium they recommend that the patient should be warned not to drink until after the local anaesthetic has worn off! Secondly, many patients have severe oesophageal obstruction and become completely obstructed when even a 14 gauge tube is inserted through the malignant stricture. It is therefore not possible to outline the lower extent of the tumour adequately if contrast material is given at this stage. Thirdly, in patients who are severely obstructed, the retained contrast medium in the proximal oesophagus makes it extremely difficult to pass the guide wire through the tumour because the tip is hidden in the pool of medium and it is often impossible to see which way it is moving.

We localize the tumour on the treatment simulator at least 24 h before attempting to pass the bougie. The length of oesophagus to be treated is determined, the centre marked with a skin mark and at the time of intubation a radio-opaque marker is placed on this skin mark. This allows us to position the applicator correctly under fluoroscopic control. The vast majority of patients have no retained contrast material in the oesophagus by the time of intubation.

Burt et al recommend the use of a 14 gauge nasogastric tube and make no mention of oesophageal dilatation. In our experience oesophageal dilatation done prior to intubation speeds the palliation of dysphagia which is consolidated and maintained by the intraluminal irradiation. The oncologist does the dilatation immediately prior to intubation and it rarely adds more than 15 min to the length of the procedure, particularly if the dilators are introduced over a guide wire.

There is now considerable experience of the effect of intra-oesophageal brachytherapy on the normal oesophageal mucosa using the 8 mm diameter applicator, and an increasing body of data accumulating from the use of the 6 mm applicator. As the therapeutic dose is usually prescribed at a distance from the central axis of the source, it is apparent that the dose to the mucosa lying against the surface of the 6 mm applicator is higher than that on the surface of the 8 mm applicator. It is not yet clear whether this is associated with a higher incidence of symptomatic damage to the normal mucosa, but the benefits of intraluminal irradiation will be reduced if patients have significant odynophagia due to mucosal ulceration. The use of a 14 gauge applicator (4.7 mm diameter) increases the risk of significant morbidity in the normal tissues still further.

We routinely combine intracavitary irradiation with external beam treatment and are currently entering patients into a trial in which the intracavitary irradiation is randomized to be given either before or after the external beam treatment. If, as occasionally happens, we are unable to intubate a patient before the external beam treatment, this can usually be achieved afterwards and, using the techniques outlined above, we have been unable to intubate only six patients in the last five years. Ten patients treated with the low-dose-rate Selectron were unable to tolerate the tube for the planned duration of treatment which had to be stopped prematurely. All of these patients received more than 70% of the planned dose. We have occasionally found that, when there is acute angulation caused by a tumour at the gastro-oesophageal junction, it has been possible to pass the guide wire into the stomach but the relatively stiff bougie would not pass around this angulation. In all cases we were able to intubate these patients successfully after they had received a course of external beam irradiation.

Yours, etc.,
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References

BURT, P. A., NOTLEY, H. M. & STOUT, R. 1989. A simple technique for intraluminal irradiation in oesophageal tumours using the high-dose-rate Microselectron. *British Journal of Radiology, 62,* 748–750.

FLORES, A. D., STOLLER, J. L., NELEMS, B., HAY, J. & JACKSON, S. M., 1987. Combined primary treatment of cancer of the esophagus and cardia by intracavitary and external irradiation. In *Diseases of the Esophagus* (Springer-Verlag, New York), pp. 745–753.

Quality assurance of ultrasound test objects

THE EDITOR—SIR,

A recent survey on ultrasound tissue equivalent test objects carried out by the Institute of Physical Sciences in Medicine clearly shows these objects to have limited useful lifetimes with deterioration setting in within 1 year of purchase. Many faults in these tissue equivalent test objects are owing to moisture loss and the resultant shrinkage of the gel. While faults within these test objects can become obvious from the ultrasound image, an alternative means (quality assurance of test objects) should provide additional useful information.

In this department we perform on a 6-monthly basis X-ray computed tomography (CT) imaging of our test objects, taking slices at 1 cm intervals. This provides a clear picture of the integrity of the test object and allows for some anticipation of replacement date. In addition, CT imaging offers good acceptance testing of these objects and will show discrepancies in the dimensions of internal structures.

We recommend this simple but effective evaluation procedure to users of ultrasound test objects who have access to X-ray CT facilities.

Yours, etc.,
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IPSM ULTRASOUND TOPIC GROUP, 1989. Ultrasound test object survey. *HPA Bulletin, June 1989,* 11–12.

1990, *The British Journal of Radiology*, *63*, 585–588

Proceedings of the British Institute of Radiology

Radiobiology proffered papers

Abstracts of papers presented at a meeting of the BIR at 36 Portland Place, London W1N 4AT, on Friday, 23 February 1990

Radiosensitivity of human tumour cell lines assessed in the adhesive tumour cell culture system, by C. S. Parkins and G. G. Steel
The effect of LET on the radiation response of human tumour cell lines of differing radiosensitivity, by J. Peacock, C. S. Parkins, G. G. Steel, R. Britten and H. Warenius. Abstract not received
The acute response of mouse kidney cells after fractionated irradiation assayed by colony formation in primary culture, by Y.-M. Jen and J. H. Hendry
Pathogenesis of radiation nephropathy: morphological studies in the pig, by M. Wooldridge, M. E. C. Robbins, M. Rezvani, S. J. Golding and J. W. Hopewell
The effect of myeloablation on the subsequent engraftment and homing of haemopoietic precursor cells in long-term cultures, by J. G. Bierkens, J. H. Hendry and N. G. Testa
Radiosensitization *in vivo*: oral (po) dosing with RSU 1069 or RB 6145 maintains potency but reduces toxicity compared with parenteral (ip) administration, by S. Cole, I. J. Stratford, E. Wright, J. Nolan and G. E. Adams
Repair, redistribution and repopulation: the relative importance in determining the acute response of the skin to fractionated irradiation, by G. J. M. J. van den Aardweg and J. W. Hopewell
Dose and field-size related changes in the thickness of the dermis after β-irradiation in the pig, by V. K. Sieber, J. C. Heryet and J. W. Hopewell
Proliferation in CaNT tumours during and after fractionated radiotherapy assessed by local control, clonogenic survival and cell kinetics, by J. J. Pavy, A. Rojas, R. J. Hodgkiss, G. D. Wilson, J. M. Collier, E. J. Kelleher, C. A. Whitsed and M. C. Joiner
Radiation and drug sensitivity measured with the MTT assay, by J. A. Hanson, D. P. Bentley, A. E. Bean, J.-A. Garnet and J. L. Moore
Cellular and molecular approaches to intrinsic radioresistance in human malignant glioma, by G. Ross, R. Brown, T. Wheldon, R. I. Freshney, R. Rampling and A. Barrett

Radiosensitivity of human tumour cell lines assessed in the adhesive tumour cell culture system

C. S. Parkins and G. G. Steel
Institute of Cancer Research, Sutton, Surrey

The adhesive tumour cell culture system (ATCCS) has been proposed as a predictive test for radiosensitivity because of its short culture period, selective growth of tumour cells and because it is thought to yield a result which reflects the clonogenic cell response. We have compared the radiosensitivity of a range of human tumour cell lines using the ATCCS and clonogenic survival. We found that the optical method of assessing cell number and radiosensitivity gave good agreement with clonogenic response at 2 Gy, although the ATCCS response showed unusually high radioresistance at high doses. The relationship between the cell number seeded and optical density was not always linear within individual assays and we prefer to use the term "slope ratio" for the derived radiation response, *e.g.* SR_2 and not SF_2. The assay could distinguish the radiosensitivity of cervix carcinoma cells ($SF_2 = 0.7$; $SR_2 = 0.74, 0.80$) from neuroblastoma cells ($SF_2 = 0.3$; $SR_2 = 0.30, 0.41$). The use of the cell-adhesive-matrix (CAM) coating on the supplied culture surface did not significantly improve colony-forming efficiency. Results are also presented for the growth and radiosensitivity of xenograft and biopsy tumour samples.

The acute response of mouse kidney cells after fractionated irradiation assayed by colony formation in primary culture

Yee-Min Jen and Jolyan H. Hendry
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It has been shown that the α/β ratios for early- and late-responding tissues are different, being around 5–20 Gy for the former and 2–5 Gy for the latter. The underlying cause for this difference could be the time available for cellular repair prior to the fixation of potentially lethal damage. Using primary culture and a clonogenic assay, mouse kidney cells after single dose, 2-, 8- and 16-fraction irradiations were assayed for their survival 12 h after single or fractionated irradiations. When the data sets were fitted separately to a linear-quadratic model the α component was constant for all regimens of irradiation. Using a direct analysis, the α/β ratio was 4.4 ± 1.3 Gy for the three fractionated regimens plus the single-dose data set, and 2.8 ± 0.9 Gy for the three fractionated regimens only. The difference was significant ($p < 0.0001$) and the fitting excluding the single-dose data set was a better fit. The result indicates an α/β value within the range of values reported using functional kidney assays, and also suggests that the time available for repair prior to assay does not account for the low α/β ratio observed in mouse kidney.

Pathogenesis of radiation nephropathy: morphological studies in the pig

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*MRC Radiobiology Unit, Chilton, *CRC Normal Tissue Radiobiology Research Group, Research Institute, University of Oxford and †Oxfordshire Regional CT Unit, Churchill Hospital, Oxford OX3 7LJ*

The pathophysiological mechanisms responsible for the development of radiation nephropathy are ill defined. Studies of changes in renal morphology should help ascertain the cell type(s) at risk and, in conjunction with functional data, provide a basis for the development of rational protocols for the treatment and/or prevention of radiation nephropathy. Both kidneys of 13 mature 10-month-old pigs were irradiated with a single dose of 9.8 Gy of ^{60}Co γ rays. The pigs were serially killed at periods up to 24 weeks after irradiation. Kidneys were perfusion-fixed, embedded in paraffin-wax and 5 μm thick sections taken for evaluation. Changes were observed in non-glomerular and glomerular tissue within 2 weeks of irradiation. Non-glomerular lesions initially consisted of focal areas of interstitial fibrosis or tubular atrophy, predominantly in the corticomedullary region or along the path of medullary rays. Maximal damage, affecting over 50% of the cortex, was observed at 6 weeks after irradiation, and consisted of severe interstitial fibrosis, tubular atrophy and inflammatory cell infiltrate. Interstitial fibrosis involved a complete band of subcapsular tissue, with "fingers" of fibrotic tissue extending deep into the cortex. Similar changes were seen up to 24 weeks after irradiation. Glomerular changes consisted of progressive increases in PAS positive staining material in the mesangial matrix, glomerular hypercellularity with cell clumping, thickening of the capillary basement membrane and a decrease in capillary lumina. Between 12 and 24 weeks, damage increased in severity, leading to the development of completely sclerotic end-stage glomeruli which were predominantly subcapsular or juxtamedullary. There was no apparent change in the vasculature. These findings show that (a) there is no one target or dose-limiting cell and (b) the vasculature does not play a major role in the primary development of radiation nephropathy.

The effect of myeloablation on the subsequent engraftment and homing of haemopoietic precursor cells in long-term cultures

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Long-term marrow cultures (LTBMCs) reconstitute *in vitro* the privileged microenvironment which is characteristic for the intact bone marrow and which is required for prolonged haemopoiesis. As such LTBMCs provide a model to study the various aspects of bone marrow transplantation. In the present experiments, the effect of 20 Gy γ-irradiation as a modality of myeloablation on the subsequent engraftment of stromal layers in LTBMCs has been assessed and compared with the "homing" ability of haemopoietically inactive cultures. Irradiated stromal layers subsequently re-inoculated with bone marrow cells, displayed a lower supportive capacity for haemopoiesis as compared with corticosteroid deprived stromal layers. This was expressed both as reduced numbers of CFU-S and GM-CFC progenitors and a fall in non-adherent cell production. These observations may be related, at least in part, to a reduced cell homing of haemopoietic cells on the irradiated stroma. A significant decrease by 35% in the cell adhesion of factor dependent FDCP-Mix-A4 cells onto irradiated stromal layers was observed within a dose range of 10 to 20 Gy. Significantly higher doses were required to affect the sulphated GAG content in fully established stromal layers. It is therefore unlikely that the reduced capacity of irradiated stromal layers to home haemopoietic precursor cells is uniquely related to the alterations observed in the sulphated GAG content in these layers.

Radiosensitization *in vivo*: oral (po) dosing with RSU 1069 or RB 6145 maintains potency but reduces toxicity compared with parenteral (ip) administration.

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RSU 1069 is a nitroimidazole hypoxic cell radiosensitizer, which is also directly cytotoxic when reductively metabolized. RB 6145 is a prodrug of RSU 1069 with reduced systemic toxicity. The maximum tolerated dose (MTD) of RSU 1069 for C3H/He mice was 80 mg/kg (0.38 mmol/kg) ip. This MTD increased four-fold to 320 mg/kg (1.5 mmol/kg) with po administration. The MTDs of RB 6145 were 350 mg/kg (0.94 mmol/kg) ip and 1 g/kg (2.67 mmol/kg) po. Toxicity of RSU 1069 towards bone marrow stem cells was also reduced approximately four-fold after po administration; 20 mg/kg ip RSU 1069 and 80 mg/kg po RSU 1069 both reduced the surviving fraction of clonogenic CFU-A cells by 50%. No loss of intestinal crypts was detected after ip or po administration of RSU 1069. Half of the mice given the highest po dose of 320 mg/kg of RSU 1069 developed cystic kidneys, with dilation, necrosis and fibrosis of the distal tubules but no nephrotoxicity resulted from the ip administration of 80 mg/kg of RSU 1069. Even relatively low doses of RSU 1069 reduced the number of spermatids visible in histological sections of testes 4 weeks later. There was some dose sparing (about two-fold) after po administration. For RSU 1069 and RB 6145, administered by either route, the maximum reduction in the survival of clonogenic cells from intradermal, murine KHT sarcomas occurred when the drugs were given 45–60 min before 10 Gy of X rays. A range of doses of RSU 1069 or RB 6145 was administered po or ip 45 min before 10 Gy. The degree of radiosensitization by both compounds was largely independent of the route of administration. Preliminary studies with ^{3}H-RSU 1069 suggested that efficacy correlated with peak blood level of label and concentration in the tumour at the time of irradiation, which were reduced less than two-fold by po compared with ip administration. Toxicity tended to correlate with total exposure over time, which was reduced two to four-fold by po administration. Oral administration of RSU 1069 or RB 6145 may give therapeutic benefit, since dose-limiting toxicity in mice was reduced compared with parenteral administration, whereas radiosensitizing activity was retained.

Repair, redistribution and repopulation: the relative importance in determining the acute response of the skin to fractionated irradiation

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The influence of the overall treatment time in fractionated irradiation was studied in the epidermis of the pig. The absence or presence of moist desquamation was assessed after β-irradiation and dose–effect curves were fitted to the quantal data using probit analysis. Experiments were compared on the basis of ED$_{50}$ values: the dose required to produce moist desquamation in 50% of the irradiated skin fields. With an overall treatment time of $\leqslant 15$ days the iso-effect doses (ED$_{50}$) for moist desquamation were well correlated ($r = 0.99$) with the number of fractions (in the range of 1–48 F) when the data were plotted on a log–log scale and when full account was taken for any incomplete repair of sublethal damage. The slope of this Strandquist-plot was represented by a fraction-exponent (N) of 0.42. This is not significantly different from those obtained for so-called late-responding normal tissues. The results of fractionated irradiation given in 1–10 F were well fitted by a Fe-plot suggesting an α/β ratio of 8.7 ± 0.5 Gy. However, the data for irradiation given in 6–48 F suggested a significantly lower α/β ratio of 0.85 ± 0.3 Gy. Comparison of the ED$_{50}$ values for irradiation given as 2 F/14 days with 2 F/38 days indicated a positive time factor with an increase in the iso-effect dose of nearly 40%, owing to repopulation. In contrast, 28 F/38 days compared with 28 F/14 days indicated a negative time factor, *i.e.* a dose reduction of nearly 30%. This could be explained by the redistribution of the target cells within the cell cycle. Fractionation studies on pig skin using X-irradiation also indicated that repopulation and redistribution are counteracting processes. The overall effectiveness of each varying with the overall treatment time. The presence of a significant degree of re-distribution of cells in the cell cycle conflicts with the basic concept of equal effects per equal dose fraction.

Dose and field-size related changes in the thickness of the dermis after β-irradiation in the pig

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The late response of dermal tissue to β-irradiation, from sources of 1–40 mm diameter, was assessed in pig skin 2 years after irradiation. Sources of 1 and 2 mm diameter were used to represent "hot particles" of the type encountered in accidental occupational exposures to radiation, whilst the larger sources (5–40 mm) represented the lower end of a range that might be used therapeutically. Single doses of β-irradiation, in the range 13–230 Gy, were given from $^{90}Sr/^{90}Y$ plaques of diameter of 1.0, 2.0, 5.0, 11.0, 15.0, 22.5 and 40.0 mm. At 2 years after irradiation samples of skin were fixed, 5 μm histological sections were prepared and the thickness of the dermis in irradiated skin was measured from a projected image of these sections. Comparisons were made with adjacent unirradiated control sites. The thickness of an irradiated area was expressed as a percentage of adjacent dermal thickness. A dose-related reduction in dermal thickness was found, irrespective of the diameter of the source, with a maximum, 60% reduction in dermal thickness. The dose required to produce this maximum reduction in dermal thickness for the 40 mm diameter source was 23.4 Gy whilst for the 1 mm diameter source it was 1050 Gy. After even higher doses there was a less severe reduction in the extent of dermal thinning; this was attributed to the presence of invasive fibrosis. In contrast to the acute response where a field size effect was seen using sources of 5–22.5 mm diameter there was no field-size effect for sources of 5 mm. The mean ED_{50} for $\geqslant 30\%$ reduction in dermal thickness following irradiation by sources 5 mm diameter was 18.00 ± 0.65 Gy. For the "hot particles" (1 mm and 2 mm diameter) a field-size effect was demonstrated as the ED_{50} for $\geqslant 30\%$ reduction in dermal thickness following irradiation with a 1 mm diameter source was 129.04 ± 1.17 Gy and 41.62 ± 1.17 for a 2 mm diameter source. The ED_{50} for the early radiation response of the skin, moist desquamation, following irradiation with the 22.5 mm diameter source was 27.3 ± 0.7 Gy whilst exposure with the small sources (1 mm and 2 mm diameter) produced an acute ulceration rather than desquamation with ED_{50} values of 253.7 ± 31.0 Gy and 119.3 ± 9.0 Gy, respectively. The ED_{50}s for the later dermal response occurred after exposure to lower doses of radiation than did those for acute response. Therefore, it is the late dermis tissue response that determines an acceptable level of exposure of the skin to radiation.

Proliferation in CaNT tumours during and after fractionated radiotherapy assessed by local control, clonogenic survival and cell kinetics

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The effect of overall time on tumour proliferation, during and after a course of fractionated X rays, was studied using three methods for assessing repopulation, in the mouse mammary carcinoma CaNT. *Local control*: 10 × 3.4 Gy, calculated to produce half the damage required to control 50% of tumours, were given in air over $3^{1}/_{3}$, 5 or 10 days. This partial amount of damage was "topped-up" with neutrons 1 or 8 days after the end of each regime. Preliminary analyses of the data show no significant repopulation during treatment when the overall time was extended from 3 to 10 days. This is compatible with no appreciable repopulation occurring over a 10 day treatment period or that repopulation was effectively counterbalanced by reoxygenation. By contrast, if an interval of 8 days was left, more neutron dose was required to produce the same level of effect, especially for the 10 F/10 days. *Clonogenic cell survival*: an *in vivo–in vitro* excision assay was performed using 10 F/5 days. Contrary to what was seen *in vivo*, no significant increase in tumour clonogens was detected during the first week after treatment. The total dose of 34 Gy reduced the relative clonogens per tumour down to $\sim 10^{-3}$, which was less than expected to cause half the full effect. *Cell kinetics*: using the same schedule as for the excision assay, the labelling index (LI) was determined using flow cytometric analysis of tumour cells pulse labelled with BUdR. An immediate reduction in LI during treatment was followed by a prompt but partial recovery. Control values were not achieved even by 20 days after end of treatment. An increase of G_2 cells was observed, persisting over the same period. The interpretation of the kinetic data is complicated because clonogenic cells cannot be distinguished from doomed cells.

Radiation and drug sensitivity measured with the MTT assay

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The MTT assay (Twentyman & Luscombe, 1987) has been used to determine cell response following *in vitro* exposure to radiation and drugs. Quantitatively, response measured in the MTT, colony forming and tritiated thymidine uptake assays varied, however qualitative ranking of cell lines was generally similar when assay time and conditions were optimized for each cell line. Radiation and adriamycin resulted in viable giant cells in some lines which may have been responsible for the observed plateau in response seen particularly with DAUDI cells. The MTT assay, along with a dye exclusion (D.Ex) assay, was further evaluated for the measurement of *in vitro* response of chronic lymphocytic leukaemia lymphocytes to chlorambucil. Response determined in the MTT assay on Day 6 and at a concentration of 1 μg/ml (continuous exposure) correlated with that measured in the D.Ex assay in five pre-treatment patients, but not in four treatment patients. A correlation was further seen between the D.Ex response in four treatment patients and their WBC count, indicative of clinical response. Clinical response data for the pre-treatment patients are as yet not available; however, these initial results indicate that the MTT assay may be used in determining *in vitro* cell response in this leukaemia. Low control absorbance and cell loss during aspiration of MTT, with non-adherent cell lines, were limiting factors. Addition of sodium succinate at a final concentration of 20 mM was found to increase formazan production whilst maintaining linearity in both CHO and Molt4 cells with no change noted in dose-response. The use of SDS in place of DMSO was also studied and was found, in two non-adherent lines, to give similar dose–response curves to that obtained using DMSO; however, less response was found in two adherent lines. As no aspiration step is involved, SDS may be of use with non-adherent cell lines.

Reference

TWENTYMAN, P. R. & LUSCOMBE, M., 1987. *British Journal of Cancer*, *56*, 279.

Cellular and molecular approaches to intrinsic radioresistance in human malignant glioma

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Progress in understanding mechanisms of cellular radioresistance is dependent on the identification of appropriate experimental models. Human malignant glioma lies at an extreme of clinical resistance, and it has been postulated that this may be attributable to "intrinsic" cellular radioresistance. We have assessed the acute radiosensitivity of six human glioma cell lines to megavoltage irradiation, using a monolayer colony forming assay. Data has been analysed using linear-quadratic and multi-target models of radiation action. All lines generate survival curves with broad initial shoulder (mean, Dq, 2.83 ± 0.42; $n = 4.9 \pm 1.1$), with values of alpha (mean, 0.1 ± 0.02) and SF2 (mean, 0.7 ± 0.05) suggestive of "intrinsic" cellular radioresistance, by comparison with such parameters obtained in other human tumour lines. There is evidence to implicate the rate and fidelity of rejoining of radiation-induced double strand breaks (DSB) as a determinant of radiosensitivity in mammalian cells. We are evaluating two experimental systems aiming to identify differences in DNA repair, in human tumour cells of varying cellular radiosensitivity. We are examining the ability of intact tumour cells or their nuclear extracts to rejoin plasmid DNA (pIC20H; pTKHgH), after induction of DSB within a "reporter gene" by restriction endonuclease. Pilot studies have obtained successful "reporter gene" transfection into a panel of human tumour lines covering a significant range of cellular radiosensitivity (glioma; ovarian carcinoma; neuroblastoma).

1990, *The British Journal of Radiology*, *63*, 589–594

Book reviews

Introduction to Neuroimaging. By William W. Orrison, pp. xii + 395, 1989 (Little, Brown and Company, Boston), £43.50.
ISBN 0-316-66492-8

This book outlines the imaging of the central nervous system in a single small volume. The work is structured around different imaging modalities with sections on plain radiography, computed tomography (CT) and magnetic resonance imaging (MRI) scanning, angiography, myelography and nuclear medicine. Each section includes notes on technique and brief descriptions of normal anatomy and common pathologies. There are additional chapters covering extracerebral cranial disease and paediatric neuroimaging.

The author has chosen a well balanced mix of common and rarer pathologies which are presented in a clear and lucid manner. Nearly a third of the volume is appropriately dedicated to CT and MRI scanning. The findings and relative merits of each modality in common conditions are considered together. This has been skilfully achieved and emphasizes the complementary nature of the two techniques. Recommendations as to which is the more appropriate investigation in different situations are made but these, as with those concerning the use of paramagnetic agents, are at times vague. The importance of sequence selection and its contribution to MR image contrast are emphasized in the preliminary technical notes, but few recommendations on sequence protocols are included in the subsequent subsections covering scanning in particular clinical circumstances. However, references to the current literature are plentiful and differential diagnoses have been emphasized.

The illustrations are well selected and generally adequately reproduced but some, particularly of plain radiographs, are poor. The layout is conventional and the work is relatively free of typographical errors. The book achieves its stated objective by providing an overview of the techniques employed in neuroradiology and their potential for diagnosis. It will undoubtedly be of interest to radiologists in training, to whom it is recommended, but in view of the emphasis on technique, radiological signs and differential diagnosis, it is unlikely to appeal to a wider audience.

J. V. Byrne

Mammography. Exercises in Radiological Diagnosis. By P. Haehnel and C. Kleitz, pp. vi + 137, 1988 (Springer-Verlag, Berlin, Heidelberg), DM35.
ISBN 3-540-15328-4 (Berlin)
0-387-15328-4 (New York)

Using 83 illustrative cases, this small book demonstrates the salient mammographic features of a wide range of breast abnormalities. Produced in Strasburg, a pre-eminent centre of breast imaging, the book is intended for radiologists and clinicians.

In some cases, line drawings have been used for further clarification. The illustrations are generally of a high quality, although radiographs of excised specimens would have enhanced the demonstration of subtle signs in a few cases.

The English is sometimes confusing and opaque. "Architectural rupture" or "disrupture", "harmonious breasts" and "excrecis" (excision) are probably sufficiently graphic terms to convey a general meaning. However, some of the pathological terminology, for instance "epithelioma", does not occur in standard histological classifications and may lead to confusion.

Despite these criticisms, this book will give the reader a quick, yet fairly comprehensive, survey of mammographic appearances.

G. H. Whitehouse

Bone and Joint Imaging. By D. Resnick, pp. xvii + 1330, 1989 (W. B. Saunders, Philadelphia), £125.
ISBN 0-7216-2215-1

It is with the greatest pleasure that I turn to another volume written by Professor Resnick. His previous papers and textbooks are models of clarity, expertise and erudition. In this superbly illustrated and produced book, there is less emphasis on pathology than in his multi-volume work, but all aspects of imaging techniques are considered in the introductory chapters while the chapters on the various disease entities are full and comprehensive. This book is reasonably priced considering its size, and should be in the possession of every diagnostic radiologist. I can heartily recommend it as an outstanding textbook in the field of musculoskeletal radiology.

P. Renton

Panoramic Radiology, 2nd edn. Ed. by Olaf E. Langland, Robert P. Langlais, W. Doss McDavid and Angelo M. DelBalso, pp. xvi + 440, 1989 (Lea & Febiger, Philadelphia), £42.
ISBN 0-8121-1168-0

Conventional and skeletal radiologists are usually blissfully ignorant about dental disease. The jaws, however, often reflect more widespread change and, because they bear teeth, also have distinctive local pathology.

This volume sets out to describe panoramic radiology mainly, I suspect, to dentists and dental radiologists. There is a fascinating introductory chapter on the history of panoramic radiography, of which tomography is only one type. This book is at its best when discussing the theory of rotational panoramic radiography; the detail was a little excessive for me, but a "must" for those in the field. It is an unusual textbook that covers technique, radiation dosage and even lists characteristics of available machines! The section on dental disease however is less than adequate, especially when compared with what has gone before, and could perhaps be expanded in any future edition. This would then truly be a text of distinction.

P. Renton

Small Bowel Radiology. Introduction and Atlas. By G. Antes and F. Eggemann, pp. vi + 207, 1988 (Springer-Verlag, Berlin), DM190.
ISBN 3-540-15263-0 (Berlin)
0-387-15263-6 (New York)

With the steady advance of endoscopic techniques from both ends of the alimentary tract, radiologists are turning their attention to the relatively neglected portion in between; the small intestine. As a result, a number of books have appeared in recent years, and a new addition to these ranks is this elegant publication by Antes and Eggemann. The authors are champions of the double contrast technique and in particular favour the use of high density barium together with a methyl cellulose suspension in order to gain the double contrast effect. The book is a compilation of more than 5000 such examinations performed in this way since 1979.

The authors open with an introductory chapter on how to perform the examination which contains a particularly useful section on manipulating the tube into the right position at the ligament of Treitz. The technical procedure is discussed in some detail with information about barium and methyl cellulose suspensions, flow rates, etc. Other methods of examining the small bowel are discussed briefly on p. 28, but clearly the authors' preference is for the double contrast technique with methyl cellulose.

The book is lavishly illustrated, but as the title indicates it is more in the style of an atlas with many illustrations and relatively little text. The illustrations are all of high quality and emphasize the detail that can be obtained with this form of double contrast technique. An interesting aspect which the authors refer to is the relevance of motility disorders in the diagnosis of small bowel disease, although some might question the relationship between hyperperistalsis and irritable bowel syndrome referred to on p. 127. Their point, however, is well taken that radiologists should perhaps pay as much attention to functional abnormalities of the small bowel as to the anatomical ones.

Little has been missed from this book except that lymphoma of the small intestine receives only scant attention. Apart from this, it is a comprehensive review of small bowel abnormalities as demonstrated by double contrast radiology. The only slight drawback is that it is more of an atlas than a text, but none the less it should serve as a stimulus to the potential achievement by quality radiology of the small intestine. It is thoroughly recommended.

ALAN FREEMAN

X-ray Differential Diagnosis in Small Bowel Disease: a Practical Approach. By J. L. Sellink, pp. x + 182, 1988 (Kluwer Academic Publishers, Dordrecht), £54.90; $99.50; Dfl190.00. ISBN 0–89838–351–X

I experienced a certain sense of déjà vu when I was presented with this book. The reason is simple: the cover illustration is almost exactly the same as that found on *Radiology of the Small Bowel, Modern Enterolysis Technique and Atlas* by Sellink and Miller, published by Martinus Nijhoff in 1982. This was a superb book and regarded by many as the "Bible" of small bowel radiology. It was authoritative, comprehensive and beautifully illustrated.

One's immediate reaction, therefore, is to ask why is there a need for a new book on the small bowel by this internationally known author? Dr Sellink does not mention one in his introduction, but the answer is found on the back cover of this volume. Here there is a note stating that although *Radiology of the Small Bowel* by Sellink and Miller had gained worldwide recognition it is now no longer available. This is a great pity and is presumably the main reason why Dr Sellink has chosen to produce this successor.

Comparison between the two books is therefore bound to be made. The most striking difference is, of course, size. The original volume by Sellink and Miller stretched to nearly 500 pages whereas this edition is only 182 pages long. Inflation has clearly taken its toll with the $54 for the original edition now being translated into the same number of more expensive pounds, and that for a book of less than half the size.

The introductory layout in both books is the same with chapters on the technique and performance of enterolysis. A number of illustrations are the same, particularly the line diagrams. "Common errors and failures" was found at the end of Sellink and Miller but has now been placed at a more logical site, immediately after the technique chapters.

The major difference between the two has been the layout of the chapters on pathological conditions of the small bowel. In the original text chapters were grouped around differing pathologies such as tumours, inflammatory conditions, etc. Dr Sellink now reverses this approach and considers first the radiological findings and then discusses the differential diagnosis. Thus the chapter headings are on increased wall thickness, mucosal relief patterns, etc. This is perhaps more logical and underscores the use of the subheading *A Practical Approach*. Again, many of the illustrations are the same as those which appeared in Sellink and Miller, which is fair enough as they illustrate the pathology very well. Does the system work? The answer has to be "up to a point". It is fine if there is only one pathological change, but when several abnormalities are present it becomes more difficult to distil a limited differential diagnosis out of the pages of this book. A serious disadvantage in this respect is the complete lack of an index, so that even if the reader thinks of a diagnosis, it is necessary to hunt through the book to find further references. Likewise, there are no references to original literature. This makes it a difficult book both to read and review. If a specific radiographic change is encountered the reader may obtain some help by looking it up but equally might become frustrated by the lack of an "in depth" description of the condition concerned.

It is difficult to recommend this book as it has many shortcomings when it is compared with its illustrious predecessor. It is a great shame that that volume is no longer available, and I can only suggest that if you see a secondhand edition of Sellink and Miller, you should snap it up quickly!

A. H. FREEMAN

Diagnosis and Therapy of Fetal Anomalies. Clinics in Diagnostic Ultrasound, No. 25. Ed. by John C. Hobbins and Beryl R. Benacerraf, pp. xiv + 324, 1989 (Churchill Livingstone, New York), £35.
ISBN 0–443–08609–5

This latest volume in the *Clinics In Diagnostic Ultrasound* Series gives a very comprehensive update on obstetric ultrasound with particular emphasis on the diagnosis and management of fetal anomalies. The authors are all world experts from both sides of the Atlantic.

Chapters over both the common fetal anomalies and some of the more rare ones, with particular emphasis not only on the diagnosis of the anomaly concerned, but also on prognosis. There is a separate chapter on invasive fetal therapy giving a balanced view of the development of this, and an up-to-date view of the current indications.

Inevitably in a multiauthor text there is some overlap, but there are no obvious contradictions. The quality of the images throughout the book is high, apart from some variability in the section of urinary tract anomalies. The only other disappointment in an otherwise excellent book was the confusion between multicystic and polycystic kidneys (page 147).

This book can be thoroughly recommended to all involved in antenatal ultrasound as a most up-to-date review of many of the most difficult diagnostic problems, and is particularly valuable with regard to its assessment of place of invasive fetal therapy.

D. W. PILLING

BIR Bulletin

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1990 BIR Awards

The Röntgen Prize

The Röntgen Prize is awarded to Dr P. N. Plowman, MA, MD, FRCP, FRCR, and team, for their wide-ranging contributions to the Journal in Radiotherapy and Oncology, in particular the use of Radiotherapy in the treatment of childhood malignancies and in the management of diseases of the endocrine system.

The Barclay Medal

The Barclay Medal is awarded to Dr J. T. Patton, FRCP, FRCR, MRCS, at Manchester Royal Infirmary, for his contribution to the Journal over a period of years, especially on growth disorders of bone, arthritis and metabolic bone disease.

The Barclay Prize

The Barclay Prize is awarded to Dr A. M. Davies, MB, ChB, DMRD, FRCR, at the Royal Orthopaedic Hospital, Birmingham and the General Hospital, Birmingham for his wide-ranging contributions to the Journal, predominantly in the fields of skeletal radiology and related subjects including application of computerized tomography (CT) in these areas.

The awards were presented at the Conversazione on March 21 at The Royal Institution, London.

Radiology 90
Harrogate, 11-13 June 1990

Radiology 90 News

The role of radionuclides in renal imaging in children: a review

Monday 11 June, 4.35 p.m.

While there is now a general appreciation of the differing roles of static renal imaging and functional studies in adults, there is still uncertainty, particularly among paediatricians, as to the most appropriate radionuclide imaging study in children with renal problems. The indications for each study, its timing, its advantages and disadvantages, will be reviewed at Radiology 90 in relation to the clinical problems of infection, obstruction, dilatation and trauma. The place of radionuclide cystography will be discussed. The role of radionuclide imaging in the management of renal disease in childhood will be presented in relation to other imaging techniques.

HELEN CARTY

Transrectal ultrasonography in the diagnosis and management of diseases of the prostate

Tuesday 12 June, 2.30 p.m.

Over the past few years there has been rapidly growing interest in transrectal ultrasonography (TRUS) of the prostate. The technique has been perceived by urologists as a major advance in the diagnosis and management of prostatic diseases. At Radiology 90, Dr G. J. Griffiths will demonstrate how TRUS can depict the major zonal anatomy of the gland including the periprostatic structures. The correlation of TRUS, microradiography and histopathology of matching slices of cadaver prostates will be used to support the interpretation of the ultrasonic features of normal and pathological states. In his lecture Dr Griffiths will show the results of TRUS in the diagnostic and management of patients with malignant and benign diseases of the prostate. Other clinical applications such as ultrasound guided biopsy and aspiration techniques will also be discussed.

G. J. GRIFFITHS

Drs G. J. Griffiths and H. Carty will be two of the eminent invited speakers from the UK and overseas who are giving concise review lectures on a range of subjects at the BIR's 48th Annual Congress, Radiology 90 at Harrogate, June 11–13, 1990.

Obituary: Sir Edward (Bill) Pochin

Sir Edward (Bill) Pochin died on January 29, 1990, at the age of 80, after four decades of distinguished service in the field of radiation protection.

He obtained his medical training at Cambridge, where he won a number of prestigious awards and prizes. In 1946 he became the Director of the Medical Research Council's Department of Clinical Research at University College Hospital, London, a position he held until his retirement in 1974. During those years he built up his worldwide reputation as an expert on thyroid diseases and, in particular, on the effects of irradiation of the thyroid gland. In the early 1950s it was therefore natural for the International Commission on Radiological Protection (ICRP), which had begun to function again after the second world war, to invite him to join its committee on internal dosimetry.

This was at a time when the effects of radioactive fallout from nuclear weapon testing programmes were beginning to cause concern. Over the next decade or so he played an exceedingly important role, both at national and at international levels, in evaluating the effects of fallout. In 1956 he was appointed United Kingdom delegate to the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and he continued to fill this position with great distinction until 1982.

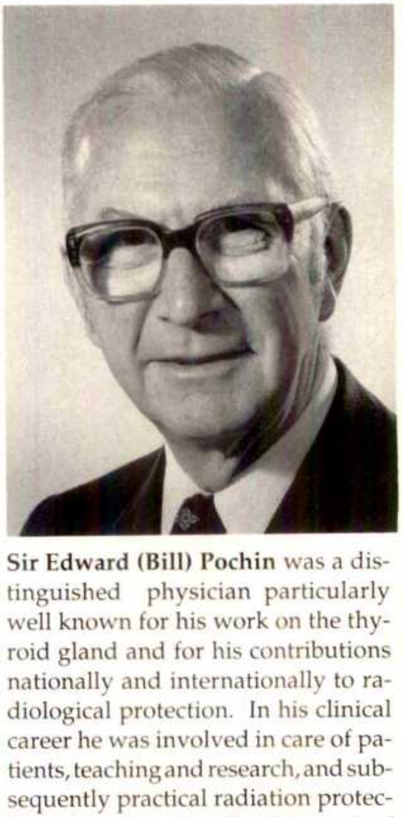
At the 1959 meeting of ICRP, Pochin was elected to the Commission; he was immediately appointed Vice-Chairman, the speediest promotion in the Commission's history. It was evident that he was being groomed for the Chairmanship after the retirement of the then Chairman, Rolf Sievert; in fact he chaired most of the Commission's meetings during the ensuing three years. In 1962 he became Chairman of ICRP, an office to which he brought all of his drive, dedication and energy. He held the post until 1969, when he once again became an ordinary member. In 1977 the Commission invited him to become an Emeritus Member, and in this capacity he attended, and took an active part in, every subsequent ICRP meeting, except for the one held a few months before his death.

In 1981 the Royal Swedish Academy of Sciences awarded him its Gold Medal for his achievements in the field of radiation protection. Amongst these, one of the most significant was his persistent drive towards quantification of radiation risk. From the late 1950s onwards he was constantly pushing his radiobiological colleagues to make numerical estimates of radiation risk, initially of leukaemia, and then of total cancer and of hereditary effects. At the same time he was personally pioneering the concept of using the ordinary risks of everyday life as a yardstick against which radiation risks could be compared. At the beginning, the comparisons that were being made were risks of fatalities, which Bill recognized as having shortcomings. He later moved forward to develop an *Index of Harm* which would take account of injuries and length of life lost, so that better risk comparisons might be made.

In 1975 he was honoured with a knighthood. Henceforth he was known publicly as Sir Edward Pochin; before that he used to sign himself as "E. Eric Pochin". However, to his family, friends and colleagues he was always "Bill". On the international scene especially, this enigmatic question of Bill's first name was a perpetual source of puzzlement.

Bill Pochin was one of those rare people who could supply enormous momentum to the work of a group. He injected ideas into discussions, and could always be relied upon to produce — on time — a draft of a paragraph/section/chapter of a document. He could be extremely tough in debate, and woe betide anyone foolish enough to enter a discussion with him with a poorly thought-out argument. However, this toughness in debate was in great contrast to the kindness and consideration he showed in informal conversation. On a personal level he could be extremely courteous and helpful; many of his colleagues can attest to, and be thankful for, the enrichment to our lives gained by exposure to this brilliant man.

David Sowby



Sir Edward (Bill) Pochin was a distinguished physician particularly well known for his work on the thyroid gland and for his contributions nationally and internationally to radiological protection. In his clinical career he was involved in care of patients, teaching and research, and subsequently practical radiation protection as well as the development of protection techniques, and in the setting of standards as well as their application.

He became an authority on endocrinology and especially on the thyroid gland. With the development of nuclear power the potential problems of the release of iodine-131, and the risk therefore to the thyroid gland, were recognized and he was well placed to study thyroid uptake, which, together with contributory studies by others, led to the use of stable iodine to block the uptake of radioactive iodine by the thyroid gland.

His reputation in this field led to his appointment as a Member of the Medical Research Council's Committee on Protection against Ionizing Radiation.

After the 1957 Windscale fire he was deeply involved in the assessment of dietary contamination; in the production of a report on exposure to external radiation; and in the interpretation of the recommendations of the International Commission on Radiological Protection to an emergency situation (the ICRP had not at that stage formulated recommendations for emergencies).

In the early 50s he became associated with the work of ICRP, becoming a full member of the Commission in 1959; he was Chairman from 1962–1969. He was also the UK Delegate to the United Nations Scientific Committee on the Effects of Atomic Radiations (UNSCEAR) from 1956 up to and including 1982. He was a member of the WHO expert advisory panel on radiation.

His standing and experience led to his becoming an Assessor for the Windscale Inquiry conducted by the Hon. Mr Justice Parker in 1977, and in 1978 he was appointed by the government to conduct an inquiry into radiological health and safety at the Atomic Weapons Research Establishment, Aldermaston. His report, always known as the "Pochin Report", led to a major overhaul in radiation protection at the Establishment.

He was a member of the National Radiological Protection Board from 1971–82 and a consultant to the Board until his death. He was a Fellow of the Royal College of Physicians and a Councillor from 1965–68.

Sir Edward's career was that of a man whose reputation nationally and internationally grew as the importance of the area in which he worked grew in relation to society. The Committees and other bodies which he chaired became immensely influential throughout the professions concerned with radiological protection, which range from the medical uses of radiation to nuclear power, and include radioactive devices in factories and consumer goods. In recognition of his individual contribution to radiological protection Sir Edward received the Sievert Award of the International Radiation Protection Association in 1984.

Sir Edward was the author of over 120 articles of chapters in medical and scientific journals or text books on thyroid disease, nuclear medicine or radiation protection. In 1982, he wrote a booklet for the International Atomic Energy Agency *Nuclear Power and the Environment* and he was also the author of a book *Nuclear Radiation: Risks and Benefits* for more general readership, published by the Oxford University Press.

It was characteristic of his dedication to the advancement of knowledge in radiation protection that after his period as Chairman of ICRP he drafted a comparative index of risks of various kinds: *Index of Harm*. He was the first in the world to try to move radiation protection on to a quantitative basis and to see how this could be used to set standards. Risk comparison of this nature was the basis of the 1977 radiation protection standards of ICRP, now in use throughout Europe, and, indeed, many other parts of the world. Although his *Index of Harm* was not perfect, no one has found anything better.

In addition to his work in the field of radiation protection he found time to travel and to draw; and his sketches of his much loved mountains provided a delightful series of Christmas cards for his many friends.

Sir Edward was created CBE in 1959 and Kt in 1975.

ROGER CLARKE

BIR Calendar

Unless otherwise indicated, enquiries about the following events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).

BIR Annual General Meeting
May 3, 1990 at 5 p.m.
36 Portland Place, London
BIR members only

The combination of chemotherapy and radiotherapy in clinical practice
May 10, 1990
All day meeting
Chairmen: Prof. A. Horwich, Dr J. Tobias and Dr S. Arnott
Speakers: G. G. Steel, A. Timothy, M. Brada, P. Hoskin, N. Plowman, P. Blake, J. R. Yarnold, D. P. Dearnaley, D. Spooner and D. Tait

The repair of radiation damage — molecules to man
May 11, 1990
All day work-in-progress meeting

Radiology 90

Harrogate, 11-13 June 1990

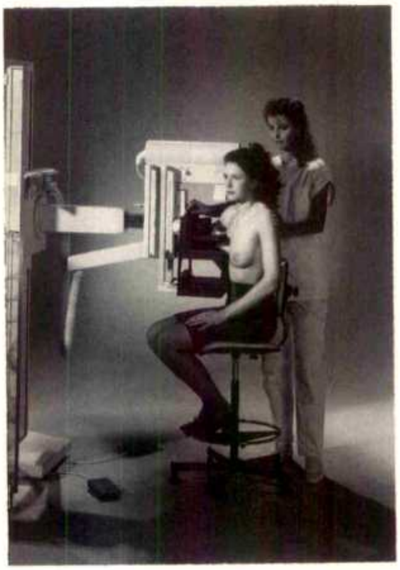
Please note that the telephone code for London is changing from 6 May 1990. The London code for the BIR will be 071 instead of 01, thus the General office will be 071-580 4089, the Editorial office will be 071-580 4189 and the Advertising office will be 071-631 1168.

The BIR fax number is also changing to 071-255 3209.

Product News

New intelligent breast biopsy guide from Smit Roentgen

The new Breast Biopsy Guide from Smit Roentgen is a removable attachment for X-ray diagnostic stands dedicated to mammography. It facilitates the accurate first-time placement of a suitable biopsy or localization needle at the site of any lesion which is detectable on the mammographs produced by the parent system. The equipment can be added on to already installed mammography units by means of simple adaptation rails.



It is an invaluable aid in the placement of such a needle, especially for lesions too small to be palpable, whether for procuring tissue samples, delivering localized treatment or placing a radio-opaque marker to assist subsequent procedures.

When a lesion in the breast is detected, it is standard practice to try to obtain tissue samples for further diagnosis, the preferred methods being either fine-needle biopsy on-the-spot, or the placing of a localization needle for subsequent surgery. With the aid of modern mammography systems, tissue changes are often detected long before they are palpable and sometimes at a very early stage when they are only a few millimetres in extent.

However, there is then a problem in follow-up, owing to the difficulty of placing the biopsy or localization needle. The Smit Roentgen Breast Biopsy Guide consists of a Guide Unit with Needle Guide Assembly and a Biopsy Data Processor Unit. Calibration marks for setting the point of needle entry are reproduced directly on the original mammograph. Depth of insertion can be accurately calculated from two simple linear measurements on one film and mechanically guided.

For further information contact Smit Roentgen, Postbox 218, 5600 MD Eindhoven, The Netherlands. Tel: 040 762707.

Philips donate X-ray unit to Romania

A mobile X-ray system, the Philips PRACTIX 21 was recently donated to the organization "Médecins Sans Frontières". The system, a powerful mobile unit suited to a wide variety of applications including paediatrics, is already in use in the Romanian city of Tirgu-Mures.

Médecins Sans Frontières is an international organization of doctors and other healthcare personnel which provides help to all victims of natural and other disasters, wars and civil disturbances, irrespective of race, political or religious belief or culture. The organization observes strict neutrality and avoids any political participation in the regions where it operates. The activities of the organization are performed anonymously and on a voluntary basis. The volunteers expect no material recompense for their services, and observe the rules of medical confidentiality. They decide for themselves whether the risks and dangers of the work are acceptable, and they require no legal protection, other than that which the organization can provide.

For further information contact Anita J. Littlechild, Philips Medical Systems Press Relations, P O Box 523, 5600 AM Eindhoven, The Netherlands. Tel: 31 40 757189.

Library News

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays).

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–7 p.m. and Thursdays 11 a.m.–5p.m. In her absence, assistance will be given by Miss Helen Smith. (Tel: 01-580 4085.)

The journal stock includes more than 100 titles. Although journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (except the historical collection) are available on loan.

Recent additions to the library

NRCP, 1988. Report No. 97: Measurement of radon and radon daughters in air.

NRCP, 1988. Report No. 99: Quality assurance for diagnostic imaging equipment.

BIR Company Subscribers

The BIR company subscriber scheme is aimed at all companies who advertise in the BJR or exhibit at the MED X RAY technical exhibition. For a subscription of £250 p.a. for an initial period of 3 years, an attractive package of benefits is offered.

If your company is interested in joining the scheme, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 01-580 4085. Companies that have enrolled to date are listed below.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex TW8 9AX; tel. 01-560 2131. Product Areas 1. Contact Mr G. Mountford, Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury, Bucks HP20 2TP; tel. 0296-395222. Product areas 4, 5, 6. Contact Mr James McLaughlin, Sales and Marketing Manager.

British Nuclear Fuels plc
Room 525, Hinton House, Risley, Warrington, Cheshire WA3 6AS; tel. 0925-835022. Product areas 8, 11. Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Cardiac Services Ltd
95A Finaghy Road, South Belfast BT10 OBY; tel. 0232-625566. Product areas 1, 3, 4, 5, 6. Contact Mr R J Brown. Managing Director.

Central Electricity Generating Board
15 Newgate Street, London EC1A 7AU; tel. 01-634 6898. Product areas 7, 8. Contact Mr R. V. Brierley, Office Services Manager.

Du Pont (UK) Ltd
Wedgwood Way, Stevenage, Hertfordshire SG1 4QN; tel. 0438 734000. Product areas 1, 3, 4, 5, 6, 7, 9 and 10. Contact Mr E. G. Lovat, Product Manager, Diagnostic Imaging.

E. G. & G. Astrophysics
Vale Road, Windsor, Berkshire SL4 5JP; tel. 0753-855611. Product areas 1, 6, 7, 8,. Contact Miss Susan Holgate, Sales Executive (Therapy).

Elscint (GB) Ltd
Tower Road, Berinsfield, Oxfordshire OX9 8LW; tel. 0865-340900 . Product areas 1, 3, 4. Contact Ms Faith Gorman, Managing Director.

E-Z-EM Ltd
1230 High Road, Whetstone, London N20; tel. 01-446 9714. Product areas 1, 2, 8. Contact Mr D. F. Wills, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London NW3 6JH; tel 01-586 9351. Product areas 1, 3. Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
4 Clarendon Chambers, Clarendon Street, Nottingham NG1 5LN; tel. 0602-483807. Product areas 1, 3, 4, 5, 6. Contact Miss Eileen Parr, Commercial Manager.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks SL1 4ER; tel. 0753-874000. Product areas 1, 2, 3, 4, 5, 6, 8, 9. Contact Jill Mitchell, UK Sales Support.

Kodak Ltd
PO Box 66, Station Road, Hemel Hempstead, Herts HP1 1JU; tel. 0442-61122. Product areas 1. Contact Mr P. E. Blackwell, Manager, Health Sciences Division.

3M UK PLC
3M House, Bracknell, PO Box 1, Berks RG12 1JU; tel. 0344 426726. Product areas 1. Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney, Northampton NN3 4RQ. tel. 0604-46132. Product areas 4, 5. Contact Mr D. G. L. Wood, Business Manager.

Medical XraySupplies Ltd
Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU; tel. 01-205 9500. Product areas 1. Contact Mr R. J. Laird, Sales Director/Managing Director.

Nuclear Associates
100 Voice Road, Carle Place, New York 11514-1593, USA; tel. 516-741 7614. Product areas 1, 3, 4, 5, 6, 8. Contact Mr H. Glasser, General Manager.

Nucletron Trading Ltd
Nucletron House, Tarporley Business Centre, Tarporley, Cheshire, CW6 9UY; tel: 0829 733611. Product areas 6, 8. Contact Mrs Marilyn A. Hart, Office Manager.

Nycomed (UK) Ltd
Nycomed House, 2111 Coventry Road, Sheldon, Birmingham B26 3EA; tel. 021-742 2444. Product areas 1, 3. Contact Mr L. Birch Hansen, Managing Director.

Philips Medical Systems
Kelvin House, 63–75 Glenthorne Road, Hammersmith, London W6 OLJ; tel. 01-741 1666. Product areas 1, 3–8. Contact J. M. Woolston, Sales and Marketing Manager.

Polaroid (UK) Ltd
Ashley Road, St Albans, Herts AL1 5PR; tel. 0727 59191. Product areas 1, 3. Contact Ms Tina Thompstone, Product Supervisor.

Premise Engineering Ltd
Tibbs Hill Road, Abbots Langley, Watford, Herts WD5 ODR; tel. 09277-67433/63320. Product areas 8. Contact Mr R. K. Beach, Director.

Quantel Ltd
Administration Centre, Kiln Road, Newbury, Berkshire RG13 2HA; tel. 0635-32222. Product areas 2, 10. Contact Mr Christopher Trim, Publicity Officer.

Schering Health Care Ltd
The Brow, Burgess Hill, West Sussex RH15 9NE; tel. 04446-6011. Product areas 1, 2, 3. Contact Mr A. Greaves, Product Manager.

Toshiba Medical Systems Europe BV
Schieweg 1, 2627 An Delft, The Netherlands; tel. 015 61 0121. Product areas 1, 6. Contact Mr. P Blonk, Office Manager, X-ray BU.

Wardray Products Ltd
Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 OSP; tel. 01-398 9911. Product areas 8. Contact Mr R. B. Wardley, Managing Director.

Key to product areas:

1. Diagnostic X-ray inc. NMR and CT.
2. Interventional radiology.
3. Ultrasound.
4. Nuclear medicine.
5. Radiopharmaceuticals.
6. Radiotherapy and oncology.
7. Radiobiology.
8. Radiation protection.
9. PACS.
10. Image processing.
11. Nuclear fuel cycle services.

Meetings and Courses

Diagnostic Imaging in Musculo-Skeletal Radiology
May 10–11
Glasgow
Further details: The Honorary Secretary,Royal College of Physicians & Surgeons of Glasgow, 242 St Vincent Street, Glasgow G2 5RJ. Tel: 041 221 6072

Carotid Duplex Technology, Hands-On Instruction
May 16–18, 1990
Dallas, USA
July 26–28, 1990
Chicago, USA
September 15–16, 1990
Northeast USA
November 1–3, 1990
Disneyland, USA
Further details: Patricia Aguilar, Keith Mauney & Associated, Inc., 600 E. Las Colinas Blvd, Suite 250, Irving, Texas, 75039, USA. Tel: (214) 402-8250.

INTERFAB 90: 39th International Trade Exhibition for Medical and Hospital Equipment and Suplies
May 15–18, 1990
Stuttgart, West Germany
Further details: Conference Secretariat, Am Kochenhof 16, Postfach 10 32 52, D-7000 Stuttgart 1.

Advanced Carotid Duplex Interpretation
May 19–20
Dallas, USA
September 18–27, 1990
Northeast USA
Further details: Patricia Aguilar, Keith Mauney & Associated, Inc., 600 E. Las Colinas Blvd, Suite 250, Irving, Texas, 75039, USA. Tel: (214) 402-8250.

International Workshop on Californium-252 Neutron Therapy: Brachy and Boron Neutron Capture Therapy
May 25–27, 1990
Lexington, USA
Further details: Ms Terry Stuart, Radiation Therapy Oncology Center, University of Kentucky Medical Center, Lexington, KY 40536-0084. Tel: (606) 233-6489.

Lower/Upper Extremity Vascular Technology, Hands-On Instruction
July 29–31, 1990
Chicago, USA
November 4–6, 1990
Disneyland, USA
Further details: Patricia Aguilar, Keith Mauney & Associated, Inc., 600 E. Las Colinas Blvd, Suite 250, Irving, Texas, 75039, USA. Tel (214) 402-8250.

The Society of Magnetic Resonance in Imaging Ninth Annual Scientific Meeting and Exhibition
August 18–24, 1990
New York, USA
Further details: SMRM Business Office, 1918 University Avenue, Suite 3C, Berkeley, CA 94704, USA. Deadline for receipt of work-in-progress abstracts: June 15, 1990.

Third International Symposium on Biliary Lithotripsy
September 13–15, 1990
Munich, West Germany
Further details: Ms J. Steinberg, Secretary to Prof. Paumgartner, Department of Medicine II, Klinikum Grosshadern, Marchioninistrasse 15, D-8000 Munich 70, FRG. Tel: 49-89-70952380.

Course on Molecular Biology for Cancer Epidemiologists
September 18–27, 1990
Lyon, France
Further details: The Unit of Education and Training, International Agency for Research on Cancer, 150, cours Albert Thomas, 69372 Lyon Cedex 08, France. Deadline for receipt of applications: 31 May 1990.

First International Congress on Very Ultra Low Dosage
September 20–22, 1990
Bordeaux, France
Further details: VULD, Secretariat, Hematology Laboratory, Faculty of Pharmacy, 3 Place de la Victoire, 33076 Bordeaux, France. Tel: 3356913424 Ext. 711. For inquiries about abstracts: Professor Ch. Doutremepuich.

23rd Annual Meeting of the European Society for Radiation Biology
September 23–26, 1990
Dublin, Ireland
Further details: Dr C. B. Seymour, Radiobiology Research Group of the Nuclear Energy Board, Geological Survey of Ireland, Beggars Bush, Dublin 4, Ireland. Tel: 01 609511, Ext. 420.

Ultrasound Angiography
September 25–28,1990
London
Further details: The Conference Secretariat, P.O. Box 15, Eastleigh, Hampshire S05 5XG.

Magnetic Resonance Imaging and Spectroscopy (Autumn Course)
October 8–12, 1990
Norway
Further details: MR-Center, The Educational Program, N7034 Trondheim, Norway. Tel: 47 7 597700.

Radiotherapy for the 90s: a Two-Day Meeting
November 8–9,1990
Manchester
Further details: B. Magee/R. D. Hunter, Radiotherapy Department, Christie Hospital and Holt Radium Institute, Wilmslow Road, Withington, Manchester M20 9BX. Tel: 061 445 8123 Ext. 293/310.

British Medical Ultrasound Society
22nd Annual Scientific Meeting
December 4–6, 1990
Harrogate
Further details: BMUS, 36 Portland Place, London W1N 3DG.

9th International Congress of Radiation Research
July 7–12, 1991
Toronto, Canada
Further details: 9th International Congress of Radiation Research, 1891 Preson White Drive, Reston, VA 22091, Canada. Tel: (703) 648-3780. Deadline for abstracts: January 15, 1991 and for Junior Investigators Awards: October 15, 1990.

As a service to our readers, notice of meetings or courses will be inserted free of charge. Please send full details to the Honorary Editor, BIR Bulletin.

Please send articles for the Bulletin or any comments or suggestions you may have about the Bulletin to The Honorary Editor, BIR Bulletin, 36 Portland Place, London W1N 4AT.

BIR Bulletin

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36 Portland Place, London W1N 4AT
The British Institute of Radiology is not responsible for opinions expressed in the BIR Bulletin

Radiology 90

Harrogate, 11-13 June 1990

New Compounds Improve Diagnostic Efficacy of MRI Examinations

Professor Bob Brasch of the University of California, USA, world renowned for his work on the development and use of contrast enhancing drugs with magnetic resonance imaging is giving a guest lecture sponsored by Schering at the Radiology 90 conference in Harrogate in June. Currently, most effort is being put into the development of Gadolinium-DTPA which is being used clinically to define abnormalities of the blood–brain barrier, to differentiate scar from recurrent disc herniation in the post-operative spine, to differentiate viable from necrotic tumour and to help characterize metastatic spread of disease. Gadolinium-DTPA is the first approved MRI contrast agent and is demonstrating high efficacy and excellent tolerance. Brasch finds the overall rate of adverse drug reactions, predominantly mild in nature, to be approximately 2.4%. Inhis lecture, he will be describing research into alternative paramagnetic agents which have a similar distribution to Gd-DTPA. he defines the ideal MRI contrast medium to include high dose efficiency, chemical stability, absence of *in vivo* metabolism of complete excretion, desired biodistribution, high solubility, particularly low cost and high tolerance. His lecture will recount efforts being made to develop MRI contrast agents to enhance the gastrointestinal tract, the functional reticuloendothial mass, the biliary system, lymph nodes and the blood pool. Bob Brasch's lecture promises to be exciting, outlining the latest developments in this new field of diagnosis.

Your chance to win a travel bursary worth up to £500!

Radiology 90 Delegates' Competition

generously sponsored by Rad Magazine

All delegates at Radiology 90 will again have the opportunity to enter a competition organized by the BIR's Industry Committee.

The main prize will be a travel bursary which you can use to attend any scientific meeting anywhere in the world.

All you need is to be registered to attend Radiology 90, answer the questions to be found in your delegates pack (available on Registration), hand in your correctly filled out answer sheet and hope to be the first to be pulled out of the hat!

MED X RAY helps to increase prizes!

Throughout MED X RAY, on many exhibition stands there will be available for collection by Radiology 90 delegates, stickers of various colours. With every type of sticker you attach to your answer sheet, the first prize that you could potentially win will rise in value.

Runners up will receive a case of champagne.

A Registrar's Adventures in Chicagoland

"Have you seen number 21?" "Where's number 9?" Exasperated queries as participants in the 1989 BIR/Rad Magazine prize quiz competition blundered into one another at Eastbourne, as we all tried to track down the various questions so cunningly distributed between the different technical stands throughout the three exhibition halls. I was delighted and amazed to win the first prize of a free trip to the RSNA in November, and so grateful to the BIR and Rad Magazine for this unique opportunity that I even agreed (in a moment of weakness) to their request that I write this short report about my visit! After all, how else could a second year radiology registrar possibly go to the RSNA without even the ordeal of having to present a paper as justification for such an indulgence?

I had not returned to the United States since living there briefly as a child when I was six years old. My most vivid memories from that period were of the wonders of Disneyland. My impressions from this current trip were not dissimilar. The RSNA is equally fantastical: a sort of gigantic radiological Disneyland where the imagery of the imagination becomes reality.

The sheer vastness of the event is mind-blowing to the uninitiated. The traffic jam of mobile MRI scanners parked nose-to-tail around the periphery of one of the technical exhibition halls almost fades into insignificance as a backdrop to the high-tech, high-finance drama being enacted on centre stage. Loath as I am to admit it, there is something about the American mentality, not to mention their resources, which enables them to execute such an extravaganza so efficiently. The organization is truly superb throughout, right down to the special congress shuttle bus service ferrying delegates from their hotels to the McCormick Conference Centre.

I found it well worth struggling in early each morning, before the buses became crowded, to profit from the opportunity of browsing round the excellent collection of scientific exhibits, which opens at 7.30 am daily. Free coffee available at this time in the scientific exhibition hall acts as an added incentive, effectively purging the mind of any excesses from the evening before and enabling full concentration on the poster presentations which are all of a very high standard. After about an hour on the scientific exhibits it is time to move off to your selected Refresher Course. These are one and a half hour sessions held at 8.30 am every morning and again at the end of each afternoon. These sessions are an absolute must, especially for any registrar attending the RSNA. They are similar to the "Teach-ins" held at the BIR Annual Congress, but obviously on a much larger scale and were relatively far better attended. Admission to a Refresher Course lecture is by allocated ticket only, sent for in advance of the Congress. It was initially frustrating agonizing over which of the many Refresher Courses to apply for, since almost all of them sounded so interesting, but in fact the choice turns out to be anything but crucial because an excellent lecture is more-or-less guaranteed, whatever the teaching topic selected. All the Refresher Course sessions I attended succeeded in providing a stimulating and concentrated synopsis of the topic in question. Particularly valuable for me was the plethora of pertinent images presented to illustrate these lectures.

Every year the RSNA runs a "Categorical Course" which seems to be very popular with American radiology residents. This comprises a series of refresher lectures all on a particular subject: this year it was paediatric radiology. The speakers produce an accompanying text which is published, complete with diagrams and radiographs, as a paperback book. Each lecture of the Categorical Course is complete in itself and may be attended as a "one off" instead of one of the other Refresher Course lectures which run concurrently.

I thought the standard of presentations at the scientific sessions was surprisingly variable, in view of the

fierce competition encountered by radiologists in getting their papers accepted for the RSNA. The total lack of any reference by our transatlantic colleagues to work already published in the British radiological literature is very striking and comes as no surprise, but the injustice of it still hurts.

One major RSNA attraction, which I think the BIR should initiate at its Annual Congress, is the Film Interpretation session. The immense "Arie Crown" — more the size of a sports stadium than a lecture theatre — was absolutely packed out from floor to ceiling. Every member of the audience was issued with a booklet containing reprints of the case histories and films whose differential diagnoses were to be discussed by members of an invited panel of experts. These "handouts" are a good idea: not only do they enable everyone to see the cases properly, but they also make any notes taken during the session seem meaningful afterwards since they accompany pictures of the films shown. I always find such film interpretations enjoyable because it is instructive to see how senior radiologists tackle a difficult case, and anyway it is rather fun to see *them* in the hot seat for a change!

Returning to Britain from RSNA Wonderland I felt rather like Alice stepping back into 'dull reality' (1) as she exclaimed, perhaps in a rather wistful voice,' "You woke me out of oh! such a curious dream; — all through the Looking-Glass world" ' (2). ' So Alice got up and ran off' (to do the barium list?) 'thinking while she ran, as well she might, what a wonderful dream it had been' (1).

Acknowledgments

I thank Professor David J. Allison and Dr A. N. Adam for allowing me the use of The Hammersmith Hospital CT scanner for frivolous purposes (outside scanning hours!).

References

(1) Lewis Carroll, 1865. *Alice's Adventures in Wonderland*.
(2) Lewis Carroll, 1872. *Alice Through the Looking-Glass*.

Nicola H. Strickland

Nycomed Scholarship 1989

I spent most of the Nycomed Scholarship at the University Hospital, Lund, in southern Sweden in the Department of Radiology where the director is Professor Anders Lunderquist. I also had the opportunity of visiting two other hospitals in Sweden during my stay: the Karolinska Institute in Stockholm and Malmö General Hospital in Malmö. During my final week I stayed in Copenhagen where I visited both the Department of Radiology at Glostrup Hospital and the William Cook factory.

University Hospital, Lund

Lund is a small university town at the southernmost tip of Sweden. The Department of Radiology at the University Hospital occupies three floors in a large central block which links the outpatient departments at one end and the wards at the other. Subspecialities within the Department of Radiology are run separately and I spent most of my visit in the gastroenterology section which is under the care of Professor Anders Lunderquist.

I learnt many things during my stay in Lund. I was particularly impressed with the central position of the radiology department, which, I think, reflects the importance that the Swedish medical profession attach to radiology, by the large amount of space available in the department and also by the efficient organization of film reporting and filing.

The lower of the three floors of the Radiology Department is occupied by the Neuroradiology Department. The middle floor consists of doctors and secretarial offices and ten large demonstration rooms. Each of these is extremely well equipped with permanent tiered seating, two viewing consoles with electronic film changers and overhead video viewing screens. Clinical sessions take place every morning between 7 and 8 o'clock in these rooms. Most medical and surgical teams have daily conferences at which both ward and pre- and post-operative patients are discussed. The films are fully discussed amongst the radiologists prior to the session, and are then presented by one of the radiologists to the clinicians. I was a little disappointed with the lack of discussion between the clinicians and the radiologists about each patient. Each session appeared concerned solely with fairly rapid presentation of the films with little or no time spent on discussing patient management or operative findings.

The top floor of the department is where the majority of both the routine and specialist investigations takes place. This floor consists of a large central corridor along one wall of which there are twelve viewing consoles with electronic film changers. Each clinical team is allocated one set of viewing boxes. As a film is processed it is immediately mounted on the viewing box belonging to the department from which that patient has been referred. Both the request form and any old films are placed with this film ready for reporting. The reporting is dictated by a radiologist, often within a few minutes of the film being mounted on the viewing box, and then one of the many technicians will send both the tape and the request form to the secretaries for typing via a vacuum pipe. The final report is usually back with the film within an hour of the radiograph being performed and in some cases only 10 minutes have elapsed before the report is ready, so that the patient is able to return with it to his doctor.

Any film which needs to be seen at the following day's clinical conference is left up on the viewing box whilst all other films are removed and filed. At the end of the day the box (or "coffin") from each viewing console, which is already loaded with the correct films, is taken to the demonstration floor below for the following day's session.

This system appeared to work extremely well almost entirely because of a large number of technicians whose sole job is to load and unload radiographs from these "coffins".

The rapid reporting and regular daily sessions are, I feel, the main reasons for the very low percentage of unavailable or "lost" old films, a statistic I would like to see emulated in my own department. The remainder of the third floor is occupied by multiple screening and general purpose rooms, ultrasound and CT scanning rooms and angiographic rooms.

Five barium rooms are used throughout the morning and the standard of the barium examinations is extremely high. Bowel preparation for the barium enema examinations consists of purgatives and no oral solids for 48 hours! Not surprisingly the colons are extremely clean. Nasogastric tubes are used for all barium meals and all examinations are performed on 100 mm spot film. Once again the efficiency within the screening rooms is notable. Patients are prepared by the radiographers/technicians, including the insertion of nasogastric or rectal catheters and the intravenous administration of bowel relaxants, before the radiologist enters the room.

Barium enema examinations are double or triple checked before the final report is issued. Each enema is provisionally reported initially by the radiologist performing the study. It is then checked by a radiologist who dictates a full report. Often a third radiologist will then recheck the examination when he comes to sign the typed report. It is extremely instructive, and a salient lesson, to see that occasionally even large polyps are missed despite this system. The interventional suite in the gastroenterology department consists of two rooms equipped with conventional C-arm and lateral screening facilities. Biliary and renal drainages and femoral, visceral and cardiac angiographic studies are performed in these rooms. During my stay a brand new Philips Digital Cardiac Imaging system was being installed in a third room for cardiac work. For the angiographic work all trainee radiologists are taught, by Anders Lunderquist, to shape catheters using a pan of boiling water and a copper wire for even simple selective angiographic studies. Although no cheaper than pre-shaped catheters, it is Anders Lunderquist's idea that this skill is an important one to learn so that a vessel not negotiable with a pre-shaped catheter can still be cannulated; an angiographer brought up to use pre-shaped catheters alone would be at a disadvantage when such a situation arose.

There is an extremely large and well equipped research laboratory at Lund shared by the Radiology and Surgery Departments. A project that Professor Lunderquist and his team have been involved in is the investigation of oily contrast media, one of which is an intravenous oily emulsion, Intraiodol, which is intended for use during computed tomography as a liver specific contrast agent. This media is based upon the parenteral feed intralipid and, following intravenous infusion, is taken up by the hepatocytes. Previous intravenous oil based emulsions have been associated with side effects which have limited their clinical use. I was extremely interested and impressed when watching Professor Lunderquist's team using vital microscopy of the rat liver to visualize directly the effects of different agents on the hepatic parenchyma. Amongst other observations they have found that the kupffer cell swelling seen with some of the other oil based contrast media, which has prevented their approval for routine clinical use, is not observed with Intraiodol.

Twenty patients have now received Intraiodol in Lund during computed tomographic examinations without significant side-effects and with excellent hepatic enhancement. Further clinical studies are now awaiting FDA approval of this agent.

Malmö

Malmö General Hospital is older than the University Hospital in Lund and consists of numerous separate buildings spread over a fairly large area. The Radiology Department is in one such building. Dr Thomas Fork, consultant radiologist in this department, allowed me to visit for several days during my stay in Sweden. He is a skilled endoscopist and therefore has the enviable opportunity of performing both barium examinations and endoscopies on patients, and is thus able to compare directly the merits and disadvantages of each of these examinations.

I will long remember his office in which he has one wall adorned with a variety of metallic foreign bodies, including knives, forks and razor blades, which had been successfully retrieved by him at endoscopy.

The Karolinska Institute

Dr Ohlsen, at the Karolinska Institute in Stockholm, runs the Interventional Department within the Department of Radiology. He has a particular interest in renal work, and especially in percutaneous stone removal. He is fortunate to have biplane screening, which I am sure facilitates the important initial renal puncture, but which is also extremely useful for locating small residual stones which cannot be seen by the nephroscopist. Dr Ohlsen has several impressive radiographs of patients with multiple, simultaneous renal punctures and tract dilatations for complete clearance of large staghorn calculi.

Once again, like the University in Lund, the department is blessed with a large amount of space and excellent modern equipment.

Glostrup Hospital, Copenhagen
My wife, who is also a radiologist, joined me for my last week in Scandinavia. After a day spent taking a final look at the sights of Lund, we travelled by ferry to Copenhagen.

Dr Pebren Ahlgren, the consultant neuroradiologist at Glostrup Hospital in Copenhagen, kindly showed us around his department. The Ultrasound Department is run by a physician, Dr Jan Pedersen, a man whose enthusiasm for his work is highly infectious. Like all the ultrasound departments that I visited in Sweden and Denmark, the standard of the work is high; I was surprised, however, to note that the interest being shown in Doppler studies in the UK is apparently not, at present, shared by the Scandinavians.

I thoroughly enjoyed my visit to Sweden and Denmark and I learnt a great deal from my stay. In particular I found out how difficult it is to watch other radiologists doing interventional procedures for six weeks and not have the opportunity to "put hands on"!

I would especially like to thank Professor Lunderquist for his teaching and for his patience when answering my questions, Dr Krassi Ivancef for his extreme hospitality, William Cook International for the immensely informative and interesting visit to their factory in Denmark and finally Nycomed for this marvellous opportunity to visit several departments in Scandinavia. I highly recommend this scholarship to any radiologist in training.

James E. Jackson

BIR Calendar

Unless otherwise indicated, enquiries about the following events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-580 4085).

The combination of chemotherapy and radiotherapy in clinical practice
May 10, 1990
All day meeting
Chairmen: Prof. A. Horwich, Dr J. Tobias and Dr S. Arnott
Speakers: G. G. Steel, A. Timothy, M. Brada, P. Hoskin, N. Plowman, P. Blake, J. R. Yarnold, D. P. Dearnaley, D. Spooner and D. Tait

The repair of radiation damage — molecules to man
May 11, 1990
All day work-in-progress meeting

Radiology 90
Harrogate, 11-13 June 1990

Library News

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays).
The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–7 p.m. and Thursdays 11 a.m.–5p.m. In her absence, assistance will be given by Miss Helen Smith. (Tel: 071-580 4085.)

The journal stock includes more than 100 titles. Although journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (except the historical collection) are available on loan.

Recent additions to the library

Semple, J., Gibb, D. et al, 1989. The place of panormaic tomography in dental radiography.
Whitehouse, G. H. & Worthington, B. S., 1990 (Eds). Techniques in diagnostic imaging, 2nd edn.

BIR members might be pleased to know that there is an agreement which allows limited use of the RSM library for reference purposes, including photocopying and searches.

Members should apply to the BIR librarian, Mrs Gunnel Ingham, for a visitor's card.

Please note that the telephone code for London is changing from 6 May 1990. The London code for the BIR will be 071 instead of 01, thus the General office will be 071-580 4089, the Editorial office will be 071-580 4189 and the Advertising office will be 071-631 1168.

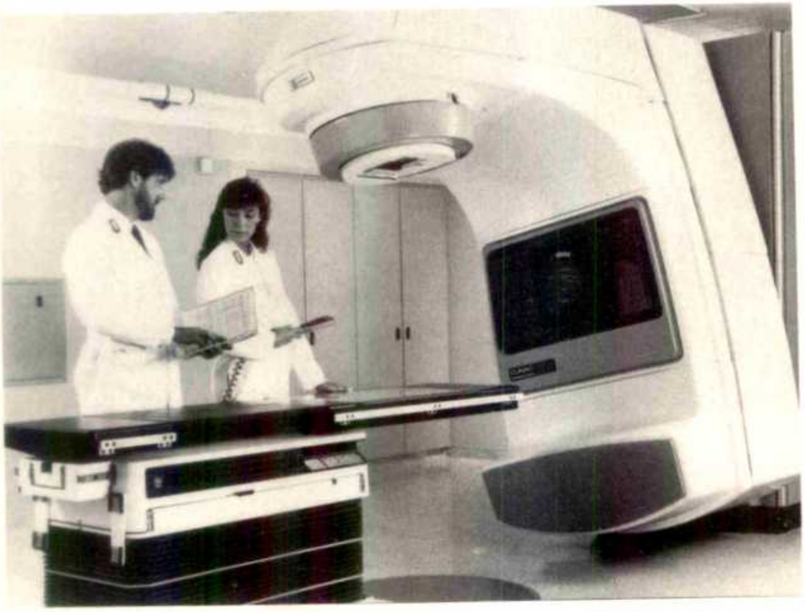
The BIR fax number is also changing to 071-255 3209.

Curt Westman Scholarship

Members wishing to visit the clinic in Vallingby, Sweden, of the late Dr Curt Westman, now owned by AB Medicinsk Rontgen, should write to the General Secretary of the BIR. Return air fares and 2 weeks' accommodation are generously provided by AB Medicinsk Rontgen, and the BIR provides a sum towards expenses.

Product News

Royal Marsden Hospital buys Varian Radiotherapy Equipment



Varian will supply a Clinac 2100C and Clinac 600C Medical Radiotherapy Accelerators and a multileaf collimator for the new cancer therapy unit currently under construction at the Royal Marsden. The order is worth over £1.8 million.

Following four months of evaluation including visits to other installations around the world, Varian equipment was chosen for its reliability. Dr Clive Harmer explained "We have a heavy throughput of patients who are referred to us locally, nationally and also from abroad. We could not afford to have a machine or machines which were not totally reliable."

The Royal Marsden will be using Varian's equipment in several specific research programmes. The multileaf collimator is a device used for shaping radiation fields in order to maximize dosage to the tumour while minimizing dose to the immediately adjacent healthy tissues.

More than 1400 Clinac accelerators are in use around the world treating some 46,000 patients daily. Varian has the world's largest installed base of radiotherapy equipment and supplies leading cancer treatment centres throughout the world.

For further information please contact Varian TEM, Gatwick Road, Crawley, West Sussex RH10 2RG. Tel. 0293 31244.

Vertec Introduce Major Advance in Mammography

The Instrumentarium Alpha III, an innovative X-ray mammography unit from Vertec Scientific represents a major technological advance in the early detection of breast cancer.

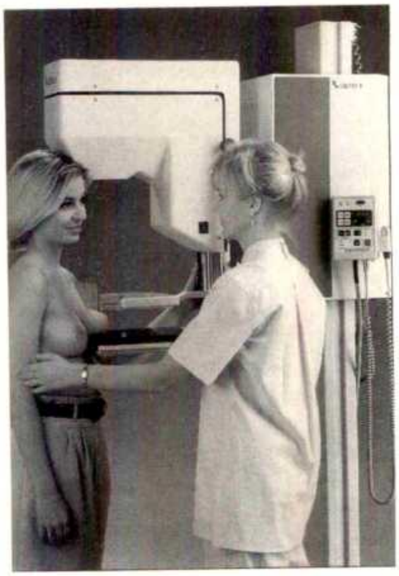
Although the system is new to the UK, it has a proven track record and has captured a 10% share of the world market since its introduction in 1988.

The system overcomes exposure related problems due to differences in thicknesses and types of breast tissue and the use of different voltages. the Alpha III's high-frequency generator and unique automatic exposure control produce superb quality images first time, eliminating time-consuming retakes and reducing patient exposure.

The Alpha III offers greater comfort for the patient with motorized or manual compression and automatic release after each exposure, thus minimizing compression time. It is microprocessor-controlled, ensuring both its own reliability and safe patient examination by continuous self-monitoring, automatically alerting the operator to any malfunction.

The Alpha III's light weight and minimal space requirements make installation simple whether used in a fixed location or as a mobile unit.

For further information contact David Piper, Vertec Scientific Ltd, 5 Comet House, Calleva Park Estate, Aldermaston, Reading, RG7 4QW. Tel. 0734 817431.



Low Energy X-Ray Therapy Seminar

A seminar entitled "Current and Future Practice and Technology in an International Context", sponsored by E G & G Astrophysics, was recently held at The British Institute of Radiology. Sixty radiotherapy professionals heard nine papers presented by prominent British and American speakers. Mr Charles Pattie, of the Oldelft Corporation of America chaired the Morning session. Miss Pauline Chalkidou gave an overview of current practice at the Royal Free Hospital and Mr Viv Whitton, Principal Physicist at the Princess Royal Hospital in Hull spoke of his own personal experience of using high frequency generators in superficial therapy equipment.

Dr Charles Coffey, of the University of Kentucky Medical Centre delivered two papers dealing with the problems involved in evaluating the beam parameters of a superficial therapy unit, and on the adaptation of the Papillon technique for use with the Therapax HF150T. Both papers were well received and inspired a great deal of interest.

Richard Clements explained modifications that the Medical Physics Department of the Cumberland Infirmary have made to their superficial unit to enable treatment of larger fields — such as those found in the case of recurrent breast tumours — which would normally be treated using an orthovoltage unit. Delegates were then reminded of the importance of the backscatter factor in dose determination by Dr Stan Klevenhagen, who explained his extensive work in that field.

In the second half of the meeting, chaired by Dr Klevenhagen, emphasis was placed on the medical aspects of the subject. Dr Margaret Spittle covered the use of low energy X rays at St John's Hospital for Diseases of the Skin for the treatment of both benign and malignant conditions, as well as discussing alternative forms of treatment. Dr Stephen Knowles from the Middlesex presented a revealing paper on the AIDS-related Kaposi's Sarcoma.

Finally, Dr Harold Hope-Stone compared the use of superficial and orthovoltage X rays with electron therapy based on his experience at the London Hospital.

A booklet of the day's proceedings is currently in production.

Further details may be obtained from Miss Susan Holgate, Therapax Sales Executive, EG&G Astrophysics, Vale Road, Windsor, Berks SL4 5JP. Tel. 0753 855611.

Kodak continues support for MRI Research

Kodak recently announced the continuation for a further four years of their support for Sir Godfrey Hounsfield's research. Since 1983 he has undertaken research into MRI at the National Heart and Chest Hospitals in London.

Current projects include 'one-shot imaging' which it is envisaged will be completed shortly, and long term investigation into 'imaging flow in coronary arteries'.

Stephen Lee, Manager, Diagnostic Imaging, said of the announcement, "His research is making a great contribution to the fundamental aspects of MR scanning. Kodak Limited and Health Sciences in particular, are pleased to be able to assist in ensuring this important work continues by providing essential back-up for Sir Godfrey until 1993."

For further information please contact Robert Ashby, Marketing Communications, Health Sciences Division, Kodak Ltd, P O Box 66, Station Road, Hemel Hempstead, Herts HP1 1JU. Tel. 0442 61122 Ext. 44480.

Protecting X-ray Films

Keeping X-ray films in a pristine condition presents certain problems, especially when they are in current use. Tyvek X-ray wallets, from Emerson Envelopes, can help solve this problem. Tyvek is a spun-bonded olefin synthetic material from Du Pont which is far stronger than paper. The X-ray wallets are antistatic, dust and lint free and have twice the normal opacity to guard against light damage. Tyvek is rot-proof and damp-proof which means it can save money through reuse, and it can be easily stored.

A standard Tyvek X-ray wallet measures 17.5" x 14.5" (444 mm x 368 mm) and can be overprinted with individual hospital details. The wallets can be ordered in quantities of as few as 1000.

For further information contact Mrs Caroline Ilott, Marketing Executive, Smith & Young Ltd, 40 Crimscott Street, London SE1 5TP. Tel. 071-231 1261.

Reactor Experiments Inc. is pleased to announce the availability of the 43rd edition of their newsletter the NEW-TRON. This humorous newsletter is published with a focus on interesting applications of Reactor Experiments' products including their metal foils and neutron/gamma shielding materials.

NEW-TRON Issue No. 43 includes articles on the production of special Borated Polyethylene for Idaho National Engineering Lab, a review of the reasons for using Alloy Activation Foils & Flux Wires, a review of the Criticality Dosimeter design, as well as descriptions of a special Neutron Source/Shipping Storage Cask and a new Isolator Material for storage of fissile materials.

For a free copy of the NEW-TRON, please write to Reactor Experiments Inc., 963 Terminal Way, San Carlos, CA 94070 or call (415) 592 3355 or FAX (415) 598 9555.

New Format Black and White Printer

The UP-930, Sony UK's latest addition to its extensive range of video printers, is a new black and white thermal printer which can produce large format prints, up to A4 in size.

This multiscan printer offers a high speed print facility, taking between 22 and 26 seconds per copy, and is capable of operating from any equipment which can provide a Red, Green and Blue (RGB) or composite video signal. The multiscan feature means that the UP-930 is able to scan a much wider range of frequencies, 15–50 KHz, which enables the user to produce a print from, for example, a computer.

With 128 gradations per dot the UP-930 offers a near photographic quality high contrast print, producing a detailed hard copy which is ideal for research and archive purposes. A two megabyte memory enables the printer to store up to eight images on a single sheet. This multiformat feature is invaluable when a comparison of several images is required, and could be issued to great advantage in ultrasound or nuclear medicine. The new large A4 format is an ideal size to be placed in patient or general medical records, particularly when recording images from X-ray, MRI or CT scanners, where an instand print is required. Other likely applications include gamma cameras, electron microscopy, position emission tomography, digital subtraction analysis and in catheterization labs.

For further information contact Caroline Kershaw, Sony Broadcast and Communications UK, Jays Close, Viables, Basingstoke, RG22 4SB. Tel. 0256 483663.

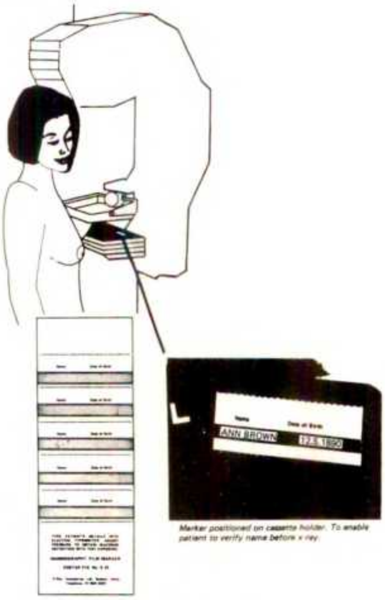
Use of Institute facilities

Readers are reminded of the availability for hire of the Lecture Theatre, Foyer and Library. Affiliated societies are offered a discount.

The Lecture Theatre holds up to 100 people in raked seating and has excellent audio-visual equipment, including VHS video. The Foyer provides space for registration and refreshment breaks for 40 people. The Library, with its beautiful Adam ceiling, can accommodate up to 60 people for refreshment breaks or for an evening reception.

Enstar Mammography Film Markers

Enstar Mammography Film Markers are designed to enable mammograms to be indelibly marked with the patient's name and date of birth or number. The details are typed on the markers using an ordinary typewriter. As the patient's breast is positioned on the cassette holder the marker is placed beside it and the patient is asked to verify her name before the film is exposed. The film is thus marked in front of the patient by the actual X-ray exposure used to make the mammogram. This eliminates the possibilities of confusion which can arise when the cassette is taken out of the presence of the patient for marking, as with standard marker strips used with actinic/light markers or with separate X-ray marking devices. No expensive X-ray marking equipment or metal plates are required, and a second marker strip can be left in place to identify the Screening Unit and date of screening. Markers are supplied in packs of 100 strips of five and will be widely available throughout the UK and overseas in 1990.



Marker positioned on cassette holder. To enable patient to verify name before x-ray

For further information contact Tony North, X Ray Accessories Ltd, 16 Rudolph Road, Bushey, Herts WD2 3DY. Tel. 01-950 2233.

BIR Company Subscribers

The BIR company subscriber scheme is aimed at all companies who advertise in the BJR or exhibit at the MED X RAY technical exhibition. For a subscription of £250 p.a. for an initial period of 3 years, an attractive package of benefits is offered.

If your company is interested in joining the scheme, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 01-580 4085. Companies that have enrolled to date are listed below.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex TW8 9AX; tel. 01-560 2131. Product Areas 1. Contact Mr G. Mountford, Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury, Bucks HP20 2TP; tel. 0296-395222. Product areas 4, 5, 6. Contact Mr James McLaughlin, Sales and Marketing Manager.

Bard Ltd
Forest Houe, Brighton Road, Crawley, West Sussex RH11 9BP; tel. 0293 27888, ext. 2204. Product area 2. Contact Anna Shores, Product Manager.

British Nuclear Fuels plc
Room 525, Hinton House, Risley, Warrington, Cheshire WA3 6AS; tel. 0925-835022. Product areas 8, 11. Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Cardiac Services Ltd
95A Finaghy Road, South Belfast BT10 OBY; tel. 0232-625566. Product areas 1, 3, 4, 5, 6. Contact Mr R J Brown. Managing Director.

Central Electricity Generating Board
15 Newgate Street, London EC1A 7AU; tel. 01-634 6898. Product areas 7, 8. Contact Mr R. V. Brierley, Office Services Manager.

Du Pont (UK) Ltd
Wedgwood Way, Stevenage, Hertfordshire SG1 4QN; tel. 0438 734000. Product areas 1, 3, 4, 5, 6, 7, 9 and 10. Contact Mr E. G. Lovat, Product Manager, Diagnostic Imaging.

E. G. & G. Astrophysics
Vale Road, Windsor, Berkshire SL4 5JP; tel. 0753-855611. Product areas 1, 6, 7, 8,. Contact Miss Susan Holgate, Sales Executive (Therapy).

Elscint (GB) Ltd
Tower Road, Berinsfield, Oxfordshire OX9 8LW; tel. 0865-340900 . Product areas 1, 3, 4. Contact Ms Faith Gorman, Managing Director.

E-Z-EM Ltd
1230 High Road, Whetstone, London N20; tel. 01-446 9714. Product areas 1, 2, 8. Contact Mr D. F. Wills, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London NW3 6JH; tel 01-586 9351. Product areas 1, 3. Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
4 Clarendon Chambers, Clarendon Street, Nottingham NG1 5LN; tel. 0602-483807. Product areas 1, 3, 4, 5, 6. Contact Miss Eileen Parr, Commercial Manager.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks SL1 4ER; tel. 0753-874000. Product areas 1, 2, 3, 4, 5, 6, 8, 9. Contact Jill Mitchell, UK Sales Support.

Kodak Ltd
PO Box 66, Station Road, Hemel Hempstead, Herts HP1 1JU; tel. 0442-61122. Product areas 1. Contact Mr P. E. Blackwell, Manager, Health Sciences Division.

3M UK PLC
3M House, Bracknell, PO Box 1, Berks RG12 1JU; tel. 0344 426726. Product areas 1. Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney, Northampton NN3 4RQ. tel. 0604-46132. Product areas 4, 5. Contact Mr D. G. L. Wood, Business Manager.

Medical XraySupplies Ltd
Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU; tel. 01-205 9500. Product areas 1. Contact Mr R. J. Laird, Sales Director/Managing Director.

Nuclear Associates
100 Voice Road, Carle Place, New York 11514-1593, USA; tel. 516-741 7614. Product areas 1, 3, 4, 5, 6, 8. Contact Mr H. Glasser, General Manager.

Nucletron Trading Ltd
Nucletron House, Tarporley Business Centre, Tarporley, Cheshire, CW6 9UY; tel: 0829 733611. Product areas 6, 8. Contact Mrs Marilyn A. Hart, Office Manager.

Nycomed (UK) Ltd
Nycomed House, 2111 Coventry Road, Sheldon, Birmingham B26 3EA; tel. 021-742 2444. Product areas 1, 3. Contact Mr L. Birch Hansen, Managing Director.

Philips Medical Systems
Kelvin House, 63–75 Glenthorne Road, Hammersmith, London W6 OLJ; tel. 01-741 1666. Product areas 1, 3–8. Contact J. M. Woolston, Sales and Marketing Manager.

Polaroid (UK) Ltd
Ashley Road, St Albans, Herts AL1 5PR; tel. 0727 59191. Product areas 1, 3. Contact Ms Tina Thompstone, Product Supervisor.

Premise Engineering Ltd
Tibbs Hill Road, Abbots Langley, Watford, Herts WD5 ODR; tel. 09277-67433/63320. Product areas 8. Contact Mr R. K. Beach, Director.

Quantel Ltd
Administration Centre, Kiln Road, Newbury, Berkshire RG13 2HA; tel. 0635-32222. Product areas 2, 10. Contact Mr Christopher Trim, Publicity Officer.

Schering Health Care Ltd
The Brow, Burgess Hill, West Sussex RH15 9NE; tel. 04446-6011. Product areas 1, 2, 3. Contact Mr A. Greaves, Product Manager.

Toshiba Medical Systems Europe BV
Schieweg 1, 2627 An Delft, The Netherlands; tel. 015 61 0121. Product areas 1, 6. Contact Mr. P Blonk, Office Manager, X-ray BU.

Wardray Products Ltd
Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 OSP; tel. 01-398 9911. Product area 8. Contact Mr R. B. Wardley, Managing Director.

Key to product areas:

1: Diagnostic X-ray including NMR and CT; 2: Interventional radiology; 3: Ultrasound; 4: Nuclear medicine; 5: Radiopharmaceuticals; 6: Radiotherapy and oncology; 7: Radiobiology; 8: Radiation protection; 9: PACS; 10: Image processing; 11: Nuclear fuel cycle services.

Meetings and Courses

Magnetic Resonance Imaging and Spectroscopy (Spring Course)
May 28–June 1, 1990
Norway
Further details: MR-Center, The Educational Program, N7034 Trondheim, Norway. Tel: 47 7 597700.

Liver Imaging: Past and Future Trends in MRI and CT
June 25–27, 1990
Boston, USA
Further details: Joseph T. Ferrucci, Department of Continuing Education, Harvard Medical School, Boston, MA 02115, USA. Tel: 617 732-1525

14th Leeds Gastroenterology Course for Radiologists
July 2–6, 1990
Leeds
Further details: Miss P. Kentley, Postgraduate Dean's Office, Level 7, Worsley Medical Building, University of Leeds, Leeds LS2 9JT. Tel: 0532 431751.

Killingbeck Cardiovascular II
July 11–13, 1990
Leeds
Further details: Dr M. R. Rees, Course Organizer, Killingbeck Hospital, York Road, Leeds LS14 6UQ. Tel: 0532 648164.

The Bart's/London FRCR Revision Course (MCQs, Film Reporting and Practice Vivas)
August 28–30, 1990
London
Further details: Mrs C. Burrage, Course Secretary, Room 26, Dunn Laboratories, St Bartholomew's Hospital, London EC1A 7BE. Tel: 071-601 7531.

4th Annual Meeting of the European Society of Head and Neck Radiology
September 12–15, 1990
Brescia, Italy
Further details: The Organizing Secretariat, Clas International S. r. l., Via Pace, 8, 25122 Brescia, Italy. Tel: 9 30 48006.

Third Annual Applied Ultrasound: Accent on Doppler
September 12–15
California, USA
Further details: Dawne Ryals, Ryals & Associates, PO Box 1925, Roswell, CA 30077-1925. Tel: 404 641-9773.

Interventional Neuroradiology: Current Practices and Techniques
September 16–18, 1990
Baltimore, USA
Further details: Program Coordinator, The Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205. Tel: 301 955-2959.

Edinburgh 90: The Royal College of Radiologist's Annual Scientific Meeting and Exhibition
September 18–21, 1990
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG. Tel: 01-636 4432. Abstract deadline: April 20, 1990.

Radiology in Britain and Belgium
September 23–30, 1990
Eastbourne and Brussels
Further details: Mrs Betsy Birchenough, Department of Radiology, University of Connecticut Health Center, Farmington, CT 06032, USA. Tel: 203 679 3322.

The Oxford Course in ENT Radiology
September 28–29, 1990
Oxford
Further details: Mrs S. Cook, Academic Secretary, Department of Otolaryngology, The Radcliffe Infirmary, Oxford OX2 6HE.

Training and Qualifications in Radiation Protection
October 2, 1990
London
Further details: Dr D. N. S. Dixon, Programme Committee Secretary, The Society for Radiological Protection, 67 Oatlands Park, Linlithgow, West Lothian EH49 6AS. Tel: (031) 244 2779.

Riyadh Armed Forces Hospital Third International Course on Magnetic Resonance Imaging
October 14–17, 1990
Riyadh, Saudi Arabia
Further details: Department of Medical Studies, Armed Forces Hospital, PO Box 7897, Riyadh 11159, Kingdom of Saudi Arabia. Tel: 9661 477 7714, Ext. 2289/2269

The Third Somerset Magnetic Resonance Imaging Course
October 29–November 1, 1990
Gwent
Further details: Rachael Amesbury, The Somerset MRI Centre, Kerland Clinic, Marsh Lane, Nr Bridgwater, Somerset TA6 6LQ. Tel: 0278 429094 (afternoons).

Advanced Oncology: Head and Neck Cancer
November 23–24, 1990
London
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London W1N 4DG. Tel: 071-323 3100.

The Seventh International Conference on Chemical Modifiers of Cancer Treatment
February 2–5, 1991
Florida, USA
Further details: Ms Suzanne Bohn, Projects Coordinator, American College of Radiology, 1101 Market St, 14th Floor, Philadelphia, PA 19107, USA. Tel: 215 574-3181. Abstract deadline: September 21, 1990.

6th World Congress in Ultrasound
September 1–6, 1991
Copenhagen, Denmark
Further details: Torben Larsen, Department of Gynecology, Herlev Hospital, DK-2730 Herlev, Denmark.

European Congress of Radiology '91
September 15–20, 1991
Vienna, Austria
Further details: The Congress Secretariat ECR '91, c/o Vienna Academy of Postgraduate Medical Education and Research, Alser Straße 4, A-1090 Vienna, Austria

As a service to our readers, notice of meetings or courses will be inserted free of charge. Please send full details to the Honorary Editor, BIR Bulletin.

Please send articles for the Bulletin or any comments or suggestions you may have about the Bulletin to The Honorary Editor, BIR Bulletin, 36 Portland Place, London W1N 4AT.

BIR Bulletin

Honorary Editor, BIR Bulletin: D. Rickards, LRCP, MRCS, FFR(D)SA, FRCR
Please address all correspondence to: Honorary Editor, BIR Bulletin, The British Institute of Radiology,
36 Portland Place, London W1N 4AT

The British Institute of Radiology is not responsible for opinions expressed in the BIR Bulletin

Aardvarks, Apes and Alligators and the BIR's 28th Conversazione

The Royal Institution in Albermarle Street with its venerable, if sombre, corinthian portals played host to the 28th conversazione of the BIR, held on the wet and blustery first evening of spring. Any members and guests who had difficulties parking in the area would be amused to learn that after the Royal Institution was opened in 1799, the popularity of the lectures was such that the traffic jams created by coaches and horses led to the creation of London's first one-way street!

The evening began with a sherry reception in the Long Library, presided over by a large oil painting of William Bragg, the discoverer of protein structures, imparting his scientific wisdom to the children at one of the famous Christmas lectures during the 1950s.

Members and guests then moved on to the intimate calm of the famous Lecture Theatre. The President, Professor Hill, welcomed members and their guests and drew attention to the debts that the science of radiology owed to discoveries made at the Royal Institution. Sir Humphrey Davy (better known to school children for his invention of the safety lamp) discovered barium and the Royal Institution's most famous son, Michael Faraday, laid the foundations for modern radiology with his discoveries on the nature of electricity and magnetism.

The BIR Awards and Honorary Memberships were then presented (details of these and profiles of award winners and new Honorary Members follow).

Professor Hill then introduced Mrs Olivia Wilson, veterinary radiographer, who has done much pioneering work at London Zoo, who gave us an amusing and illuminating lecture entitled "Aardvarks, apes and alligators — ultrasound and X-ray at London Zoo".

Mrs Wilson began by explaining some of the more obvious differences between working with animals and humans. Size, for instance, is a more greatly variable factor with "patients" ranging from tiny possums to hefty rhinos. Language is another problem, but Mrs Wilson described how it is possible to establish a good rapport with an animal through gentle handling. Lucy, the marmoset, for instance, would allow herself to be stretched out on a little wooden cross for her ultrasound examination and Mrs Wilson assured us that snakes were especially capable of a good rapport with their handler. Mrs Thatcher, however, was not easily convinced of this on her visit to London Zoo when she met the rather ominously named Grey Rat Snake!

Mrs Wilson went on to describe other problems in animal radiography. Elephants, for instance, have exceptionally thick skin. She described how determining a pregnancy through ultrasound required the whole of the radiographer's arm, up to the shoulder, to be placed in the animal's rectum — an extremely painful experience when the muscles in the rectum continue to contract even under sedation! The examination of rhinos has similar drawbacks. One patient, examined by Mrs Wilson for an ovarian check after failing to become pregnant, turned out to be a sterile male!

Other "heavy-weight" patients included a lion, X-rayed to determine why his legs were growing apart. Mrs Wilson's beautiful radiograph revealed a spine very like a human spine but with calcification on the discs. When the lion began to wake up prematurely, he had to be hastily injected by Mrs Wilson and her team. Since different animals react individually to sedation levels, radiographing has to be quick in order to avoid possible death or the early waking of a rather grumpy, slumbersome animal!

The most spectacular ultrasound examination undertaken by Mrs Wilson, however, was on the two killer whales, Nimo and Freya. An animal with such large organs (the liver is 3 feet long and 2 feet deep) obviously presents great practical problems in examination. Mrs Wilson ended up spending a day in the pool with the whales with a Siemens portable scanner perched precariously overhead. Unfortunately, Nimo's spleen problem resulted in death but Freya's abscess was curable.

Some of Mrs Wilson's most interesting slides were of reptile radiographs. The most beautiful was of an iguana with a fractured femur showing the delicate flow of its limbs and curvacious claws. The fracture was cured by pegging the femur. It came as something of a surprise to learn that reptiles, like humans, suffer from rickets, leading to weakened bones, possibly as a result of a dietary deficiency.

Examining cold blooded animals has its own peculiar problems. Energetic, scuttling lizards were made suitably sophorific by a spell in the fridge, while bigger specimens were consigned to two and a half hours in the cold room dustbin. And those still dubious about the wisdom of eating eggs lightly boiled may be interested to hear that one good bite from a chameleon can result in a bout of salmonella poisoning.

Mrs Wilson rounded off the lecture by telling us about her favourite patient — Edwina the Aardvark, with whom she had had a particularly trusting relationship. Since the aardvark is a nocturnal animal, its ovarian cycle had not been studied. Mrs Wilson undertook an ultrasound examination of Edwina following her two failed pregnancies. Edwina's third pregnancy was successful and Mrs Wilson's final slide was of the infant aardvark, complete with her excess folds of skin — nature's ready made garment to grow into!

In an age when animal experimentation has done so much for the health of mankind, it was heartening to see, through Mrs Wilson's work, how radiological techniques could be used to the benefit of the animal world. Mrs Wilson ended by giving special thanks to Professor George du Boulay for his support of her work.

Guests then proceeded back to the Long Library for a cosily hearty buffet supper with wine. Tours were then organized of the museum in the basement, dedicated to the achievements of Michael Faraday.

When the Royal Institution was founded in 1799 by Count Rumford, former British intelligence agent and employee of the Elector of Bavaria, its aim was to facilitate "the application of science to the common purposes of life". In keeping with this, the town house in Albemarle Street was bought (the Corinthian facade did not appear until 1838) and its facilities included an exhibition of heating stoves, similar to those used by Rumford himself to feed beggars at a soup kitchen in Munich. It was the lecturing and research brilliance of Sir Humphrey Davy which turned the Royal Institution into a more professional and fashionable centre for learning about new scientific discovery. But one of Davy's greatest contributions to science was, possibly, his discovery of Michael Faraday, the blacksmith's son, whose experiments at the Royal Institution into electro-magnetic induction laid the foundation of the modern electrical industry. In the museum, guests were able to see a replica of his laboratory, looking like something out of the world of Professor Brainstorm with quaint gadgets and tiny coloured bottles. Faraday's electro-magnetic induction coil, which resulted in the world's first transformer, as well as a replica of the device used for experiments into electro-magnetic rotations, which led to the creation of the world's first electric motor, were on show as well as original notebooks and papers. Faraday's scientific legacy is, in fact, even with us in our language. Together with a Cambridge don, Faraday coined words "anode, cathode, electrode" and even the word "scientist". It was he too who began the Christmas lectures for children, the popularity of which has made the Institution's beautiful lecture theatre familiar to homes throughout the country.

There was much to learn about then that evening — from the joys of elephant ultrasound to Faraday's electrical experiments. And next time you just happen to be snarled up in London's one-way system, remember, that was a "first" for the Royal Institution as well!

R. A. HAYNES

BIR Awards

Barclay Medal

Dr J. T. Patton

Professor C. R. Hill presenting the award to Dr Terry Patton

Dr J. T. Patton, affectionately known as Terry, qualified from the University of Liverpool in 1951 and undertook house jobs locally, including orthopaedics, which has proved to be a lifelong interest. From 1952 to 1954 Dr Patton did his National Service in the Royal Navy and was appointed to the Royal Naval Orthopaedic Unit at Haslar Hospital, Gosport. He subsequently remained in the Royal Naval Reserve, retiring in 1978 as Surgeon Captain with the Reserve Decoration. From 1976 to 1978 he held the position of Honorary Physician to the Queen.

Dr Patton's interest in matters maritime was furthered during a period as Medical Officer with the Cunard Steamship Company from

1954 to 1956, serving on North Atlantic passages and cruises to Scandinavia, the Mediterranean and around the world. In 1956, he started radiological training at Liverpool and it was here at the Royal Liverpool Children's Hospital, working with Dr Norah Walker, that his interest in paediatric bone disease was first stimulated. His Senior Registrarship followed in 1960 at Manchester where his new chief, Dr John Fawcitt, had the good sense to insist on his joining the BIR. Following rotations to Manchester Royal Infirmary in the early 60s he was appointed Consultant at the Manchester Royal Infirmary with a special interest in skeletal radiology, joining such notable experts as Kellgren in rheumatology, Stanbury in metabolic bone disease and Lloyd Griffiths in orthopaedic surgery. Interest in skeletal dysplasia was stimulated by working as Junior Consultant to Dr Blair Hartley at St Mary's Hospital for Women and Children. From 1979 Dr Patton has been the Consultant in Administrative Charge of radiological services at Manchester Royal Infirmary and St Mary's Hospital.

Dr Patton is a founder member of the International Skeletal Society and has been an examiner in the Final Fellowship of the Royal College of Radiologists and also examiner to the Universities of Aberdeen, London, Edinburgh, Baghdad and Malaysia. He has served as Chairman of the North English Branch of the British Institute of Radiology and as civilian Consultant in Radiology to the Royal Navy. He is currently Chairman of the Armed Services Consultant Approval Board in Radiology.

In addition to long service as a member of the Editorial Board of the *British Journal of Radiology* and recently as its Honorary Diagnostic Editor, Dr Patton has published extensively on skeletal dysplasias, metabolic bone disease, Paget's Disease, discography and spondylitis. He has contributed to many textbooks and is the author of several invited reviews of bone infection.

D. G. SHAW

Barclay Prize

Dr A. M. Davies

Professor C. R. Hill presenting the award to Dr A. M. Davies

Dr Mark Davies graduated in medicine from the University of Birmingham Medical School in 1978. At a very early stage he had decided to pursue a career in Radiology with a special interest in orthopaedics and trauma. In 1980 he joined the West Midlands Training Scheme in Radiology at the earliest possible opportunity. He fulfilled all his early promise and sailed through the radiological training at registrar and Senior Registrar levels with commendations, obtained DMRD and FRCR diplomas and in 1984, at an early age of 29 years, he was appointed as successor to Dr Phillip Jacobs as the Consultant Radiologist to the Royal Orthopaedic, Birmingham Accident and General Hospitals in Birmingham, with special interest in skeletal radiology. The University of Birmingham conferred upon him the honorary title of Senior Clinical Lecturer in Radiology.

This year's Barclay Prize is awarded to Mark Davies for his wide ranging publications in the *Britsh Journal of Radiology*. This is indeed a very well deserved honour as in just 5 years he has to his credit over 25 publications, numerous presentations, lectures and book reviews and has been asked to referee scientific papers for publication. He is a popular tutor and is always sought after by trainee radiologists for guidance in matters of research and publications. Indeed, he has encouraged juniors and consultant colleagues alike to join him in the pursuit of research ideas and subsequent publications which have followed. These activities have led him to membership of the Training Subcommittee of the West Midlands Training Schemes in Radiology, the Northwest MCQ Panel of the Royal College of Radiologists and the Editorial Board of the journal *Radiology Now*.

His principal interest is in the fields of skeletal radiology and related subjects and through his numerous publications he has demonstrated the applications and usefulness of computed tomography in these areas. He is now a recognized and well respected expert in his field, and a member of numerous national groups such as the Medical Research Council Bone Sarcoma Panel, Skeletal Radiology Group, Bone Dysplasia Group and also Naughton-Dunn Orthopaedic Club. Locally he is an Honorary Secretary and Treasurer of the West Midlands Association of Radiologists and a member of its Executive Committee.

It gives me personal pleasure in recording these achievements and gratification to have had some input, albeit very small, into Mark's meteoric progress at such a young age. The Barclay Prize of the Institute is very well deserved and I am sure more recognition will follow.

K. J. SHAH

Roentgen Prize

Dr P. N. Plowman and Team

This year's Roentgen Prize is awarded to Dr Nick Plowman and his colleagues, in particular David Doughty and Ewan Thomson, for their publications in radiotherapy and oncology over the last 10 years.

Nick Plowman graduated from Cambridge University and Guy's Hospital in 1974. He gained a double first in the Medical Sciences Tripos and a first in the Natural Sciences Tripos at Emanuel College. He then obtained an MB BChir with Honours at Guy's. After a period of general medical training at Guy's, Addenbrooke's and the Hammersmith Hospital, during which time he obtained the Diploma of MRCP, he became a Medical Research Council Research Fellow in the Department of Oncology and Radiotherapeutics at Cambridge under the Directorship of Professor Norman Bleehen. He gained an MD at Cambridge in 1980, his thesis being human macrophages and studies in human bronchial carcinoma.

During this time, his interest in radiotherapy and oncology as a career had been fired and, in 1979, he joined the Department of Radiotherapy and Oncology at St Bartholomew's Hospital with an Honorary Appointment at the Hospital for Sick Children, Great Ormond Street.

Dr Plowman's interests are wide ranging and he has an outstanding and considerable list of publications in many distinguished Journals. However, his contributions to the *British Journal of Radiology* have been of particular note. Following his appointment as Consultant in the Department of Radiotherapy at St Bartholomew's Hospital, and to the Department of Oncology at the Hospital for Sick Children, Great Ormond Street, he has developed a particular interest in the management of paediatric malignancies and in the use of radiotherapy in the treatment of a variety of endocrine disorders.

He has been responsible for pioneering work in the treatment of retinoblastoma, having developed a highly accurate beam-splitting technique of treatment which enables the lens to be spared. He was also responsible for setting up the total body irradiation and marrow transplantation programme for childhood malignancies at St Bartholomew's Hospital, and to date over 100 children have been treated in this fashion.

At St Bartholomew's Hospital, Nick Plowman has worked tirelessly to establish joint approaches with his colleagues to the management of paediatric malignancies and also endocrine disorders.

He has contributed actively to many National Health Service and Medical Research Council Committees and was responsible for organizing the Conference held at St Bartholomew's Hospital in 1987 to celebrate 50 years of mega-voltage radiotherapy at that hospital. To have achieved so much at such an early stage in his career is in itself outstanding, and it is just recognition of his abilities and those of his associates, that the Institute has awarded them the Roentgen Prize.

S. J. ARNOTT

David Doughty collecting the award on behalf of Dr Plowman and team

BIR Honorary Members

Professor J. F. Fowler

There can be few radiotherapists or radiobiologists in the United Kingdom (or elsewhere) who have not been influenced in some way by Jack Fowler. He has been at the forefront of radiobiological research as applied to radiotherapy for over 30 years, and prior to that in Medical Physics, first at Newcastle and then London. A lasting interest, among many, has been the development of the scientific basis for dose fractionation. Jack pioneered the use of pig skin as a model of human skin in pre-therapeutic studies of fractionation with neutrons at the MRC Cyclotron Unit, Hammersmith Hospital. When he moved to the Gray Laboratory as Director in 1970, Jack began a series of studies of the effects of fractionation in tumours and normal tissues which lead directly to the application of the linear-quadratic formalism in clinical practice, culminating in the design of the CHART accelerated fractionation trial recently initiated at Mount Vernon Hospital.

Jack Fowler's association with the British Institute of Radiology has been a long one. He was Secretary of the BIR Fractionation Working Party, and President in 1977–1978. His scholarship has been recognized by many national and international bodies. Among his many awards are an Honorary Degree of MD from the University of Helsinki and the Roentgen Plaque of Remscheid Museum, Roentgen's birthplace. Jack is also an Honorary Member of the American College of Radiology and the American Association of Medical Physicists. The British Institute of Radiology honours itself in electing Jack Fowler to Honorary Membership.

N. J. McNALLY

Sir Thomas Lodge

Left to right: Professor B. S. Worthington, Professor C. R. Hill and Sir Thomas Lodge

Sir Thomas Lodge is one of the doyens of British Radiology who, over the course of a long career, has made enormous contributions to the advancement of his speciality in the United Kingdom, and this was recognized by the conferment of a knighthood in 1974.

After training in radiology in Manchester he returned to Sheffield, the city where he had qualified, becoming successively first Assistant and then Consultant in Radiology. As an acknowledged leader in his profession he served the then Faculty of Radiology with distinction, first as Editor of *Clinical Radiology* and then as President from 1963 to 1966. He was Consultant Adviser to the Department of Health form 1965 until his retirement in 1974.

He has been a regular contributor to and supporter of the affairs of the BIR throughout his active career and continues his interest in the early development of radiology through current service on the historical working party. In his Mackenzie Davidson lecture in 1972 on the subject of developmental defects in the cranial vault, he alluded to his study of symmetrical thinning of the parietal bones in early human populations, in this way introducing another of his interests, that of archaeology.

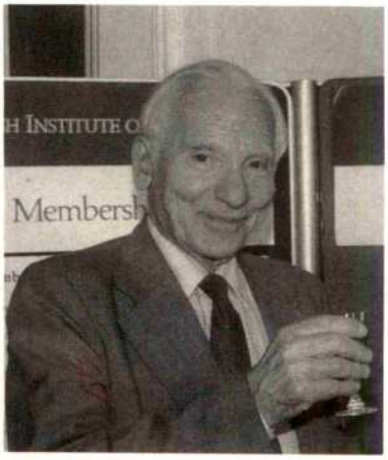
Sir Thomas is an accomplished after dinner speaker and has held many and audience in rapt attention with a flow of erudition and wit and above all the apt quotation to match the occasion.

This high standing in the International Community of Radiology has led to the conferment of Honorary Fellowships of the Royal Australasian College of Radiology in 1963, the Faculty of Radiology of the Royal College of Surgeons of Ireland in 1965 and the American College of Radiology in 1974.

Those who have had the good fortune to know him personally will concur that he makes light of his considerable attainments and many have benefited form the wise counsel of one of the outstanding leaders of our profession.

B. S. Worthington

Professor J. Rotblat



Professor Rotblat at the BIR AGM

Professor Joseph Rotblat is well known to older members of the BIR for his long tenure of the Chair of Physics at St Bartholomew's Hospital Medical College, his publications in the *British Journal of Radiology* and his active participation in BIR affairs, culminating in the Presidency during 1971–1972. However, even older members may not know the variety of Professor Rotblat's achievements in other fields. While working with Chadwick in Liverpool in 1939, he became involved in work on uranium fission and he was one of the British group that participated in work on the atomic bomb at Los Alamos. By 1944, however, he concluded that the magnitude of the project was beyond the capability of German scientists in their bombed and beleaguered country and as this removed his motive for participating he resigned, the only scientist to do so. Thenceforth he devoted himself wholeheartedly to working for the ultimate elimination of nuclear weapons. In 1955 he was the youngest signatory of the Russell–Einstein manifesto, from which sprang the Pugwash Conferences on Science and World Affairs. From 1957 to 1973, Rotblat served as the first Secretary-General of Pugwash and he is the only person who has attended all the Pugwash Conferences. In 1988 he was elected President of Pugwash in succession to Professor Dorothy Hodgkin, DM, FRS.

On the occasion of his 80th birthday in November 1988, several foreign Academies of Science honoured Joseph Rotblat by electing him into membership and in 1989 the President of the Federal Republic of

Germany conferred on him the Knight Commander's Cross of the Order of Merit of the Federal Republic. It is surely fitting that the British Institute of Radiology should recognize the distinction of one of its oldest members who has applied his scientific knowledge not only in the field of radiology but also in the wider field of world affairs by electing him to Honorary Membership.

J. W. Boag

Dr J. J. Wild

Dr John Wild must have undisputed claim to be the father figure of modern diagnostic ultrasound. After qualifying in Medicine at Cambridge in 1942, followed by war service in the RAMC, he joined the Department of Surgery at the University of Minnesota in 1946. Here, in seeking better means to assess the anatomy and pathology of problems presenting for surgery, he became aware of some novel ultrasonic echolocation equipment that was being used for purposes of radar training at a local naval air station. With characteristic energy and ingenuity, he had very soon developed and started to apply first A-scan and then B-scan imaging techniques for investigation of the bowel, breast and brain and, by 1958, for much of the time with the help only of one electronic engineer, Jack Reid, he had mapped out many of the technical features of the subject that are familiar today: grey scale, real time, intra-cavitary and tissue characterization, among others, and had pointed the way to a number of their successful clinical applications, particularly in cancer.

In all this, whilst Wild was breaking entirely new ground, he was not entirely alone in the field, and his early work was in parallel with, although apparently independent of, that of Dr Douglass Howry, a radiologist working in Denver. However, in terms of breadth and vision, certainly as evidenced by his prolific publications, there are strong grounds for seeing Wild as the outstanding pioneer. What is remarkable, with the benefit of hindsight, is the extent to which he was ahead of his time, to the point that the implications of his work were either ignored or misunderstood by virtually all his contemporaries, and its practical outcome only started to become widely available to radiologists and their patients some 15 years after Wild's research programme was abruptly closed down by an obtuse grant administration, and his equipment confiscated and destroyed. How often can prophets indeed be without honour in their own generation!

C. R. Hill

Professor C. R. Hill and Dr John Wild

Library News

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays).

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–7 p.m. and Thursdays 11 a.m.–5p.m.

The journal stock includes more than 100 titles. Although journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (except the historical collection) are available on loan.

Members can apply to the BIR librarian for a visitor's card which allows limited use of the RSM library for reference purposes, including photocopying and searches.

New Librarian

There will be a new Librarian Designate working in the BIR library starting this month. He is Mr Stephen Johnson, and will be working every day from Monday to Friday.

Please note, however, that although this will lead to a greatly improved service, the ongoing restorative work in the library means that the service will still be slightly restricted (until the end of August). We apologise for any inconvenience.

Recent additions to the library

Chisin, R., 1989. MRI/CT and Pathology in Head and Neck Tumours. A Correlative Study.

Hendriks, M. J., 1988. Computed Tomography of the Pituary Gland: an Anatomical and Pathological Study.

IAEA, 1989. Radiation Monitoring in the Mining and Milling of Radioactive Ores.

Jeffrey, R. B. Jr, 1989. CT and Sonography of the Acute Abdomen.

McLaughlin, W. L., Boyd, A. W., Chadwick, K. H., McDonald, J. C. & Miller, A., 1989. Dosimetry for Radiation Processing.

Mahboubi, S. (Ed.), 1989. Pediatric Bone Imaging. A Practical Approach.

Modic, M. T., Masaryk, T. J. & Ross, J. S., 1989. Magnetic Resonance Imaging of the Spine.

Pohost, G. M., Higgins, C. B., Nanda, N. C., Ritchie, J. L. & Schelbert, H. R. (Eds), 1989. New Concepts in Cardiac Imaging.

Priestman, T. J., 1989. Cancer Chemotherapy: an Introduction, 3rd edn.

BIR Calendar

Unless otherwise indicated, enquiries about the following events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 071-580 4085).

MRI Meeting
October 15, 1990
Middlesex Hospital
Organizer: B. S. Worthington

Cracking Gallbladder and Bile Duct Problems
October 18, 1990
All day meeting
Chairmen: R. H. Dowling and R. Dick
Organizer: Dr A. Adam, London
Speakers: R. H. Dowling, C. Russell, P. R. Mueller, W. R. Lees, D. Martin, R. Dick, I. S. Benjamin and A. Adam

Prediction and Management of Tumour Response to Treatment
November 9, 1990
Organizer: Dr R. Camplejohn

IPSM/Nuclear Medicine Radionuclide Tomography Update
November 21, 1990
All day meeting organized by IPSM

Planning for 1992 — A Review of Radiation Protection Practice in Member States of the EEC
December 5, 1990
Institution of Electrical Engineers
Organizer: Dr M. Fitzgerald

Is your Mammography up to Scratch?
January 17, 1991
Scientific Societies Lecture Theatre
Joint BIR/RCR/RSM all day meeting
Organizer: Professor G. H. Whitehouse

Cerebral Bloodflow Practical Measurement and Clinical Relevance — a Multimodality Approach
February 12, 1991
All day Meeting

CT — Are the Bells and Whistles Worthwhile?
February 20, 1991
All day meeting
Organizers: Drs A. Dixon and S. Golding

Radiobiology Proffered Papers
February 22, 1991
Organizer: Dr R. Camplejohn

Radiation Oncology/IPSM
April 10, 1991
All day meeting organized by IPSM

RADIOLOGY 91 and MED X RAY
May 2–4, 1991
Brighton

Radiation Oncology and Radiobiology: Particle Therapy
June 7, 1991

White Paper and 1992 Impact on Radiology
June 13, 1990
All day meeting
Organizers: A. Budge, J. Twydle and E. Beckmann
Chairman: Iain Watt

Moves afoot at the BIR!

There will be reorganization of accomodation over the forthcoming months (until September) to enhance the facilities available to members and visitors.

The library ceiling is being restored until the end of August. During this time, use of the library will be restricted and disrupted.

The General Secretary's Office is now in the former BMUS office on the second floor, and the Conference team, together with the General Secretary's PA, now occupy the old Siemens Room. The du Boulay Room will become the Member's room and is being refurbished. The Administration Office is now in the former Conference Office (the Jan Lewando Room), leaving the former General Office, after refurbishment, to become the new Siemens room.

It is hoped that all of these works, along with the installation of a receptionist, will be completed by the end of September 1990.

Product News

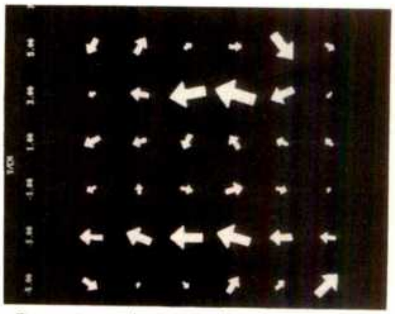
Biomagnetic Source Imaging with SQUIDS

A new method for functional brain diagnosis

Philips Research Laboratories in Hamburg will collaborate with Professor B. Bromm at the University Hospital of Hamburg on a project to investigate the cause and control of neurological pain by means of a new technique called "Biomagnetic Source Imaging".

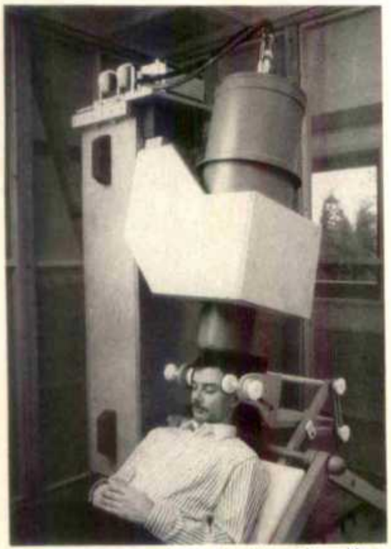
New technology, at present at the research stage, uses small magnetic fields, collected with specially wound gradiometer coils to measure the magnetic fields produced by neuronal electric activity within the human body. It is hoped that it could prove useful for research into diseases such as epilepsy, Alzheimer's disease, Parkinson's disease, schizophrenia, migraine and pain itself.

Biomagnetic Source Imaging is based on the detection of tiny magnetic fields, measurement of their magnitudes at many locations simultaneously, and three-dimensional location of their sources. The sources are, in fact, the tiny electrical currents, mostly transient, which have long been known to be intimately associated with brain activity and the nervous and motor systems throughout the body.



Reconstructed current distribution within the phantom

At the heart of the associated technology is a new solid-state device known as a SQUID (Superconducting Quantum Interference Device). It is supercooled by liquid helium to allow advantages to be gained from the "Josephson effect" giving the device a remarkable sensitivity which results in pin-point accuracy. A computer processes the results to create a display that illustrates the distribution and time evolution of electrical activity within the specific organ being examined. Compared with electroencephalography a significantly better spatial resolution of a few millimetres can be reached, and compared with positron emission tomography, the temporal resolution of about one millisecond is clearly superior.



The measuring system inside a glass fibre reinforced liquid helium dewar and the positioning unit made of wood to avoid magnetic interference

New Body Scanning Gamma Camera for Oxford

The number of patients having scans to detect cancer in bone at the Churchill Hospital, Oxford will be doubled thanks to a new high quality body scanning camera which can move underneath a special couch to take pictures without causing any distress to patients.

IGE were able to provide a suitable moving stand for the camera, linked to the latest IGE Star Computer. Instead of taking over an hour to take pictures of portions of the skeleton separately, the examination can be done in half the time with a more life-like image of the whole skeleton.

The £100 000 equipment has been bought by the Friends of the Oxford Body Scanner and the Oxford Regional Health Authority. An additional £10 000 will be needed to refurbish the isotope scanning part of the department. If anyone has any spare money and would like to donate it for these purposes, please send it to: Friends of the Body Scanner, care of Dr F. W. Wright, Churchill Hospital, Headington, Oxford OX3.

CT Scanner "Best Thing Since Sliced Bread"

Dr Oscar Craig, President of the Royal College of Radiologists, recently opened a CT Scanner facility at the Kent and Canterbury Hospital featuring a CT 9800 Hilight from IGE Medical Systems.

Dr Craig commented "It is always a pleasure to open a CT Scanner suite, the more the better, as they really are the best thing since sliced bread. This scanner, the 9800 Hilight, is the top of the IGE range and the first of its type to be installed in England".

The 9800 Hilight is configured with an independent viewing console, optical disk system and 3D facilities. For film record the CT unit has a state-of-the-art 3M Laser Camera.

For further information contact Mike Head, Heads public relations, 2 Griffin Mall, Griffin Lane, Aylesbury, Bucks HP19 3BP. Tel. 0296 392460.

New Automated Vascular Diagnostic System

Imex Medical Systems have developed an innovative peripheral vascular testing system which provides fully-automated arterial and venous tests equivalent to those done in a hospital vascular lab for clinics and small practices.

The Imex Lab9000 combines bidirectional doppler ultrasound and bilateral plethysmography technologies in a user-friendly, microprocessor based system.

For further information contact John Etter, Imex Medical Systems, 6355 Joyce Drive, Golden, Colorado 80403, USA.

In Brief

Kontron Instruments has recently appointed Drew Mowatt to head its newly strengthened Ultrasound Sales Division.

Drew joins Kontron from Dynamic Imaging as UK Sales Manager, responsible for sales of the new range of Sigma 44 High Velocity Colour Doppler ultrasound instruments.

Mark Foxall, previously with Toshiba's ultrasound sales team, has recently taken over responsibility for the promotion of Toshiba X-ray equipment in the West Midlands region.

BIR Company Subscribers

The BIR company subscriber scheme is aimed at all companies who advertise in the BJR or exhibit at the MED X RAY technical exhibition. For a subscription of £250 p.a. for an initial period of 3 years, an attractive package of benefits is offered.

If your company is interested in joining the scheme, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 071-580 4085. Companies that have enrolled to date are listed below.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex TW8 9AX; tel. 081-560 2131. Product Areas 1. Contact Mr G. Mountford, Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury, Bucks HP20 2TP; tel. 0296-395222. Product areas 4, 5, 6. Contact Mr James McLaughlin, Sales and Marketing Manager.

Bard Ltd
Forest Houe, Brighton Road, Crawley, West Sussex RH11 9BP; tel. 0293 27888, ext. 2204. Product area 2. Contact Anna Shores, Product Manager.

British Nuclear Fuels plc
Room 525, Hinton House, Risley, Warrington, Cheshire WA3 6AS; tel. 0925-835022. Product areas 8, 11. Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Cardiac Services Ltd
95A Finaghy Road, South Belfast BT10 OBY; tel. 0232-625566. Product areas 1, 3, 4, 5, 6. Contact Mr R J Brown, Managing Director.

Central Electricity Generating Board
15 Newgate Street, London EC1A 7AU; tel. 071-634 6898. Product areas 7, 8. Contact Mr R. V. Brierley, Office Services Manager.

Du Pont (UK) Ltd
Wedgwood Way, Stevenage, Hertfordshire SG1 4QN; tel. 0438 734000. Product areas 1, 3, 4, 5, 6, 7, 9 and 10. Contact Mr E. G. Lovat, Product Manager, Diagnostic Imaging.

E. G. & G. Astrophysics
Vale Road, Windsor, Berkshire SL4 5JP; tel. 0753-855611. Product areas 1, 6, 7, 8,. Contact Miss Susan Holgate, Sales Executive (Therapy).

Elscint (GB) Ltd
Colonial Business Park, Colonial Way, Watford, Herts WD2 4PT; tel. 0865-340900 . Product areas 1, 3, 4. Contact Faith Gorman, Marketing Manager.

E-Z-EM Ltd
1230 High Road, Whetstone, London N20; tel. 081-446 9714. Product areas 1, 2, 8. Contact Mr D. F. Wills, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London NW3 6JH; tel 071-586 9351. Product areas 1, 3. Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
34 Shakespeare Street, Nottingham NG1 4FQ; tel. 0602 483807. Product areas 1, 3, 4, 5, 6. Contact Miss Eileen Parr, Commercial Manager.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks SL1 4ER; tel. 0753-874000. Product areas 1, 2, 3, 4, 5, 6, 8, 9. Contact Jill Mitchell, UK Sales Support.

Kodak Ltd
PO Box 66, Station Road, Hemel Hempstead, Herts HP1 1JU; tel. 0442-61122. Product areas 1. Contact Mr P. E. Blackwell, Manager, Health Sciences Division.

3M UK PLC
3M House, Bracknell, PO Box 1, Berks RG12 1JU; tel. 0344 426726. Product areas 1. Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney, Northampton NN3 4RQ. tel. 0604-46132. Product areas 4, 5. Contact Mr D. G. L. Wood, Business Manager.

Medical XraySupplies Ltd
Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU; tel. 081-205 9500. Product areas 1. Contact Mr R. J. Laird, Sales Director/Managing Director.

Nuclear Associates
100 Voice Road, Carle Place, New York 11514-1593, USA; tel. 516-741 7614. Product areas 1, 3, 4, 5, 6, 8. Contact Mr H. Glasser, General Manager.

Nucletron Trading Ltd
Nucletron House, Tarporley Business Centre, Tarporley, Cheshire, CW6 9UY; tel: 0829 733611. Product areas 6, 8. Contact Mrs Marilyn A. Hart, Office Manager.

Nycomed (UK) Ltd
Nycomed House, 2111 Coventry Road, Sheldon, Birmingham B26 3EA; tel. 021-742 2444. Product areas 1, 3. Contact Mr L. Birch Hansen, Managing Director.

Philips Medical Systems
Kelvin House, 63–75 Glenthorne Road, Hammersmith, London W6 OLJ; tel. 081-741 1666. Product areas 1, 3–8. Contact J. M. Woolston, Sales and Marketing Manager.

Polaroid (UK) Ltd
Ashley Road, St Albans, Herts AL1 5PR; tel. 0727 59191. Product areas 1, 3. Contact Ms Tina Thompstone, Product Supervisor.

Premise Engineering Ltd
Tibbs Hill Road, Abbots Langley, Watford, Herts WD5 ODR; tel. 09277-67433/63320. Product areas 8. Contact Mr R. K. Beach, Director.

Quantel Ltd
Administration Centre, Kiln Road, Newbury, Berkshire RG13 2HA; tel. 0444 232323. Product areas 2, 10. Contact Mr Christopher Trim, Publicity Officer.

Schering Health Care Ltd
The Brow, Burgess Hill, West Sussex RH15 9NE; tel. 04446-6011. Product areas 1, 2, 3. Contact Mr A. Greaves, Product Manager.

Toshiba Medical Systems UK
Manor Court, Manor Royal, Crawley, West Sussex RH10 2PY; tel. 0293 560772. Product areas 1, 2, 3, 4, 9, 10. Contact Mr S. M. Weeden, Manager X-ray Products.

Toshiba Medical Systems Europe BV
Schieweg 1, 2627 An Delft, The Netherlands; tel. 015 61 0121. Product areas 1, 2, 3, 4, 9, 10. Contact Mr P Blonk, Office Manager, X-ray BU.

X-rite (H. Miller Graphics Ltd)
8 Moody Street, Congleton, Cheshire CW12 4AP; tel. 0260 279988. Product areas 1, 12. Contact Mrs P. Dhanani, Medical Sales.

Wardray Products Ltd
Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 OSP; tel. 081-398 9911. Product area 8. Contact Mr R. B. Wardley, Managing Director.

Key to product areas:

1: Diagnostic X-ray including NMR and CT
2: Interventional radiology
3: Ultrasound
4: Nuclear medicine
5: Radiopharmaceuticals
6: Radiotherapy and oncology
7: Radiobiology
8: Radiation protection
9: PACS
10: Image processing
11: Nuclear fuel cycle services
12: Quality assurance.

Meetings and Courses

The Bart's/London FRCR II Revision Course (MCQs, Film Reporting and Practice Vivas)
August 28–30, 1990
London
Further details: Mrs C. Burrage, Course Secretary, Room 26, Dunn Laboratories, St Bartholomew's Hospital, London EC1A 7BE. Tel: 071-601 7531.

Brachytherapy Working Conference 6th International Selectron Users' Meeting
September 9–11, 1990
Florence, Italy
Further details: Conference Secretariat, Nucletron International B. V., PO Box 110, 3956 ZT Leersum, The Netherlands. Tel: 31 0 3434 54224.

International Skeletal Society — 17th Annual Refresher Course
September 9–15, 1990
Salzburg, Austria
Further details: Secretary/Treasurer, International Skeletal Society, Radiology Department, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia PA19104, USA.

Edinburgh 90: The Royal College of Radiologist's Annual Scientific Meeting and Exhibition
September 18–21, 1990
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG. Tel: 071-636 4432.

11th Annual Study Day: the Role of the Plain Abdominal Radiograph in the Acute Abdomen
October 5, 1990
Canterbury
Further details: Postgraduate Administrator, Kent Postgraduate Medical Centre, Kent & Canterbury Hospital, Canterbury, Kent CT1 3NG. Tel: (0227) 766877, Ext. 4361.

Tutorial in Italy
October 10–15, 1990
Lake Como, Italy
Further details: Radiology Postgraduate Education Office; Cornell University Medical College, 1300 York Avenue, New York, NY 10021, USA. Tel: (212) 746 2522.

Endo-urology and Percutaneous Access Course
November 22–24, 1990
Newcastle upon Tyne
Further details: Mrs D. Lees, Teaching Centre, Freeman Hospital, Freeman Road, Newcastle upon Tyne NW7 7DN. Tel. (091) 2843111, Ext. 3051.

MRI Update
December 13–15, 1990
New York
Further details: Radiology Postgraduate Education Office, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, USA. Tel: (212) 746 2522.

1st UAE Diagnostic Radiology and Imaging Conference
January 14–17, 1991
Abu Dhabi, United Arab Emirates
Further details: Dr Abdul Rahim Jaafar, Chairman, Organizing Committee, Assistant Under-Secretary, Ministry of Health, Mafraq Hospital, PO Box 2951, Abu Dhabi, UAE. Fax: 21549.

Diagnostic Radiology in Aruba
January 20–26, 1991
Aruba
Further details: Radiology Postgraduate Education Office, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, USA. Tel: (212) 746 2522.

2nd European Meeting on Contrast Media Research
March 26–27, 1991
Lyon, France)
Further details: P. G. Promotion, 17 rue Childebert, 69002 Lyon, France. Tel: (33) 78 42 67 70.

Marie Curie Memorial Foundation 2nd International Cambridge Conference on Breast Cancer Screening
April 15–17, 1991
Cambridge
Further details: International Cambridge Conference on Breast Cancer Screening, Education Department, 11 Lyndhurst Gardens, London NW3 5NS. Tel: 071-435 4305.

8th International Workshop on Bone Dosimetry
April 28–May 2, 1991
Bad Reichenhall, Germany
Further details: Dr Deiter Felsenberg, Freie Universität Berlin, Klinikum Steglitz, Hindenburgdamm 30, D-1000 Berlin 45, Germany.

6th World Congress in Ultrasound
September 1–6, 1991
Copenhagen, Denmark
Further details: Torben Larsen, Department of Gynecology, Herlev Hospital, DK-2730 Herlev, Denmark.

6th Asian Oceanian Congress of Radiology
December 14–18, 1991
New Delhi, India
Further details: M. L. Malhotra, Executive Secretary, Aggarwal Imaging Research Centre, 10-B, Kasturba Gandhi Marg, New Delhi-110 001, India.

Third European Symposium on Uroradiology
Imaging and Intervention
August 24–27, 1992
Denmark
Further details: Henrik S. Thomsen, Department of Diagnostic Radiology 54E2, Herlev Hospital, Herlev Ringvej 75, DK-2730 Herlev, Denmark. Tel: 45 44 53 53 00, Ext. 278. Deadline for abstracts: March 1 1992.

Workshops in Radiation Physics and Radiation Biology

The L.H. Gray Memorial Trust sponsors occasional workshops along the lines of the L. H. Gray Conferences but on a smaller scale.

The Trust welcomes proposals from anyone seeking to organize a workshop in this area.

Further details: Professor G. Gordon Steele, Radiotherapy Research Department, Institute of Cancer Research, Sutton, Surrey SM2 5NG.

As a service to our readers, notice of meetings or courses will be inserted free of charge. Please send full details to the Honorary Editor, BIR Bulletin.

Please send articles for the Bulletin or any comments or suggestions you may have about the Bulletin to The Honorary Editor, BIR Bulletin, 36 Portland Place, London W1N 4AT.